NRA Special Review of

Metham Sodium, Dazomet and Methylisothiocyanate (MITC)

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Preface

The NRA report on the Special Review of Metham Sodium, Dazomet and Methylsiothiocyanate (MITC) is published as a three volume set. The contents of each volume is as follows;

Volume one

- is a record of the special review, including a regulatory history of metham sodium and recommendations for use of metham sodium and dazomet containing products in Australia.

Volume two

- provides the summary reports of the assessment of toxicological data for metham, dazomet and MITC, including a summary of comparative toxicology of the three compounds. It also contains the occupational health and safety (OH&S) risk assessment of metham (soil fumigant use) dazomet and MITC and provides recommendations for use of dazomet and soil fumigant use of metham. This volume also includes an OH&S risk assessment of root inhibitor use of metham and recommendations for use of metham as a root inhibitor.

Volume three

- contains the full reports of the toxicological assessments for Metham-Sodium, Dazomet and MITC.

FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent statutory authority with responsibility for the regulation of agricultural and veterinary chemicals. One of the NRA's regulatory responsibilities is to conduct reviews of registered agricultural and veterinary chemicals to ensure that they continue to do the job that they are supposed to do and that they do not pose unacceptable risks to people, the environment or trade.

The Special Review Program examines urgent or specific concerns about a currently registered agricultural or veterinary chemical, which may require a rapid resolution. It addresses one or more specific aspects of a given chemical, and can be triggered, for example, by the findings of new research, the availability of new scientific data or concerns raised about the use or safety of a chemical.

In undertaking reviews, the NRA works in close cooperation with advisory agencies including the Department of Health and Family Services (Chemicals and Non-Prescription Drug Branch), Environment Australia (Risk Assessment Branch), Worksafe Australia (Chemical Assessment Division) and State Departments of Agriculture.

The NRA has a policy of encouraging openness and transparency in its activities and community involvement in decision-making. When the NRA decides that a review is to be conducted, it consults parties affected by the review (such as applicants, commodity groups, State regulatory agencies) and gives them an opportunity to respond to concerns raised and participate in the review. All participants are notified of the Board's decision and outcomes of special reviews are published in the NRA's Agricultural and Veterinary Chemicals Gazette.

This review report provides an overview of the review that has been conducted by the NRA and advisory agencies. The review findings are based on information collected from a variety of sources, including data packages and information submitted by registrants, information submitted by members of the public, and government organisations and literature searches.

The NRA also makes these reports available to the regulatory agencies of other countries which are part of the OECD ad hoc exchange program. Under this program, it has been agreed that countries receiving these reports will not utilise them for registration purposes unless they are also provided with the raw data from the relevant applicant.

The information and technical data required by the NRA to review the safety of both new and existing chemical products must be derived according to accepted scientific principles, as must the methods of assessment undertaken. Details of required data are outlined in various NRA publications.

Other publications explaining the NRA's requirements for registration can also be purchased or obtained by contacting the NRA. Among these are: Ag Manual: The Requirements for Agricultural Chemicals; Vet Manual: The Requirements Manual for Veterinary Chemicals and Volume II of Interim Requirements for the Registration of Agricultural and Veterinary Chemical Products.

The NRA welcomes comments on this review and its review program. They can be addressed to Manager, Chemical Review, National Registration Authority for Agricultural and Veterinary Chemicals, PO Box E240 Kingston ACT 2604 Australia.

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Metham & Metham-Sodium Summary

SUMMARY

Introduction

Metham (and its sodium salt, metham-sodium) is a dithiocarbamate soil fumigant with fungicide, nematocide, herbicide and insecticide activity. Its activity is due to its rapid decomposition in soil to methylisothiocyanate (MITC). This decomposition is a chemical rather than a biological process. There are several end use products (EUPs) containing metham-sodium registered for use in Australia. They are used for a range of crops, including ornamentals, food and fibre crops and tobacco. Some of the EUPs are used as inhibitors of root growth in sewer lines. Metham is in Schedule 6 of the SUSDP. The Department agreed to clearance of metham sources in August, 1991. No ADI has been set.

Metham-sodium has been placed on the National Registration Authority's Ad Hoc Review Program following a report of adverse effects to an Victorian orchardist who experienced severe eye irritation and nausea when using metham-sodium to fumigate soil. This evaluation consolidates all available toxicological data which have been submitted by a range of companies between 1986 and 1991.

Metabolism and Toxicokinetics

MITC is likely to be the main metabolite of orally-administered metham, although no data were presented to support this. This supposition is based on the fact that both metham and dazomet are broken down in soil to MITC, and that after oral administration of [^{14}C]dazomet to rats, a volatile compound, presumably MITC, accounted for the majority of radioactivity in hepatic portal vein plasma.

Methyl and other alkyl isothiocyanates are excreted in the urine of rats as mercapturic acid derivatives following oral administration of metham-sodium.

Acute Toxicity

Metham-sodium has moderately high acute oral and moderate dermal toxicity, with lowest oral LD_{50} values of 50 mg/kg (mouse), 100 mg/kg (cat), and 450 mg/kg (rat), and lowest dermal LD_{50} values of 650 mg/kg (rat) and 800 mg/kg (rabbit). Acute inhalation toxicity was low in rats with an LC_{50} >4700 mg/m^3.

Metham-sodium (37% aqueous solution) produced severe skin irritation to rats and rabbits and the technical material was corrosive to rabbit skin. As a 3% aqueous solution, metham-sodium produced slight skin irritation in rats and rabbits. Metham-sodium (as a 3% or 37% aqueous solution) was a moderate eye irritant to rabbits. It was a moderate to strong skin sensitiser in guinea pigs.

Short Term Repeat Dose Studies

No short term, repeat dose studies with metham-sodium are available.

Subchronic Toxicity

In an inhalation study in rats, doses of up to 160 mg/m^3 metham-sodium for 6 h/day for 5 d/week for 13 weeks did not result in mortalities, but decreased food consumption, bodyweight, serum albumin concentration and increased relative liver weights were seen at the highest dose level. No effects were seen at doses up to 45 mg/m^3.

Chronic Toxicity

No chronic studies on metham-sodium are available. However, 2-year carcinogenicity studies with the metabolite, MITC, administered in drinking water, have been conducted. MITC was not carcinogenic in mice at doses up to 27 mg/kg/d or in rats at doses up to 1.6 mg/kg/d (males) or 2.7 mg/kg/d (females).

Reproductive Toxicity

The only available data from reproductive studies are from a published paper in which metham-sodium was given orally to rats at a dose of 1/20 LD_{50} prior to implantation and during pregnancy or for one month after parturition. No adverse effects were observed in the progeny of treated dams.

Developmental Toxicity

In a rat developmental toxicity study, maternotoxicity was noted at oral doses of 40 and 120 mg/kg/d, with decreased food consumption and weight gain. Foetotoxicity was noted at 40 and 120 mg/kg/d, with reduced foetal weights and reduced placental weights. There was a significant increase in skeletal variations at 120 mg/kg/d, possibly due to foetal immaturity, and foetal skeletal retardations at 40 and 120 mg/kg/d, corresponding to decreased foetal weights at these doses. There were 2 foetuses (out of 261 foetuses) from 1 litter at 120 mg/kg/d with meningocoele, a rare abnormality. In a range-finding study, this abnormality was seen in 12 foetuses from 7 litters at 240 mg/kg/d. Thus, meningocoele appears to occur in a dose-related manner in the rat, with an NOEL of 40 mg/kg/d. The overall NOEL was 10 mg/kg/d.

In a rabbit developmental toxicity study, maternotoxicity was seen after oral dosing at 100 mg/kg/d, and embryotoxicity was noted at 30 and 100 mg/kg/d po, and was characterised by increased post-implantation loss at both doses. There was also a low incidence (2/48 foetuses (from 2 litters)) of rare abnormalities (spina bifida or meningocoele) at 100 mg/kg/d. These abnormalities were not observed at a dose of 200 mg/kg/d in a range-finding study. The NOEL was 10 mg/kg/d.

Genotoxicity

Metham-sodium was negative for genotoxicity in a range of *in vitro* and *in vivo* assays, both with and without metabolite activation, with the exception of a human lymphocyte *in vitro* assay, where chromosome damaging effects were noted both with and without metabolic activation. Chromosome aberrations were not induced in *in vivo* studies.

Human Studies

In a published paper, there was a report of 15 cases of contact dermatitis following the use of a 10% VAPAM formulation by an unspecified number of workers in an occupational setting. Skin irritation was moderate to severe. Subsequent exposure to lower concentrations of metham-sodium (down to 1.5% VAPAM) caused skin reactions suggesting sensitisation, although the non-irritating concentration of VAPAM was not determined for use in the challenge test.

The acute health effects of metham-sodium released in a railroad transport accident in northern California were described in a published paper. Reported health effects in residents of a nearby town included non-specific neurologic complaints (headache and dizziness) and irritation (eye, respiratory tract, gastrointestinal tract and skin), and were consistent with MITC exposure. Nausea was also commonly experienced. 14% of residents sought medical attention, but in nearly all cases, symptoms were not severe enough to warrant hospitalisation. Reliable air data for the first 2 days after the spill were not available, but modelling by these authors suggested that the highest air concentrations of MITC in the town were less than 160 ppb. Another published paper reported on the longer-term health effects following the spill. Persistent respiratory health complaints were identified in 48 patients (2.3% of the town's population). A futher paper described the risk assessment process used following the spill and the authors estimated that the range of MITC concentrations immediately after the spill was 140-1600 ppb.

DISCUSSION

The toxicology data package for metham-sodium is relatively limited. A proportion of the data submitted was from poorly conducted and/or documented studies, and detail of methodology was frequently lacking. Minimal toxicokinetic and metabolism data were submitted. Whilst it is known that metham breaks down in soil to MITC, there is no information on its conversion to MITC by metabolism in animal tissues, although this would appear to be likely. It is noteworthy that the related chemical, dazomet, which also breaks down in the soil to MITC, would appear to be largely absorbed (at least in rats) as MITC following oral administration.

No chronic or short term repeat dose studies were submitted and reproductive toxicology data were minimal. However, as human exposure to metham is associated with systemic exposure to MITC, then these limitations in the data package for metham are overcome by the available data on the systemic toxicity of MITC and dazomet (see toxicological reports attached). For both of these latter compounds, data are available concerning short term repeat dose toxicity, subchronic toxicity, chronic toxicity, carcinogenicity and reproductive toxicity. Moreover, there was no evidence that these compounds had carcinogenic activity or affected reproductive performance. Target organs of metham toxicity were not clearly identified in the package of data on metham because of the lack of appropriate studies. Given the considerations discussed above, it is likely that appropriate studies would have identified the liver and red blood cells as targets of metham toxicity (given that these were identified as targets of dazomet and/or MITC toxicity). Indeed, the 13-week inhalation study of metham-sodium in rats suggested that the liver is a target organ (increased relative liver weights and decreased serum albumin concentration).

As noted above, metham-sodium is not stable when present in its EUP form and it rapidly breaks down to MITC, a highly volatile chemical. Because of this instability and because MITC is phytotoxic, especially to young seedlings, it has, in the past, been considered questionable whether exposure of the human population to metham (or MITC) via food residues is an issue. As is the case for MITC, no ADI has been set as PACSC recommendations were that an ADI is not relevant. Nevertheless, it is noted that the MRL Standard (ref. 26) does contain MRLs for metham.

In an occupational setting, systemic exposure to metham is possible via the dermal route. There are no data to indicate the extent of percutaneous absorption of the chemical or the extent of dermal metabolism. The most serious acute effects of metham appear to be severe to moderate skin and eye irritation and strong skin sensitisation both in humans and in laboratory animals. From the chemistry of metham-sodium, occupational exposure is most likely to the volatile breakdown product, MITC, rather than to metham itself. The effects of such exposure to MITC would be expected to be comparable to (or possibly more serious than) direct exposure to metham, because MITC is a severe skin and eye irritant and causes skin sensitisation. Additionally, it should be noted that MITC has a local irritant effect on the lung following inhalational exposure. Furthermore, inhalational or dermal absorption of volatile MITC may result in systemic exposure, although no data are available on the extent of absorption of MITC by these routes. By-stander exposure, as well as occupational exposure, to MITC may occur following the use of metham-sodium, because of the volatility of MITC. The risk associated with such exposure is difficult to quantify because of lack of relevant data, in particular ambient concentrations of MITC following the use of metham-sodium (which may vary considerably depending on the weather conditions at the time of use). This issue should be addressed by WSA using exposure modelling.

As noted above, such exposure could result in eye, skin and lung irritation (because of the high irritancy of MITC) and possible systemic exposure to MITC following dermal or inhalational absorption, depending on the a number of factors such as the amount applied, the method of application, weather conditions, proximity to the site of application. It should be noted that the orchardist who lodged the complaint that led to the review of metham-sodium noted that his mother, who was inside the house at the time that he was applying metham-sodium, detected the vapour. The distance that the house was from the site of application was not stated precisely ("at some distance away"). The woman apparently did not suffer any adverse effects.

Of note are the rare abnormalities detected in both rat and rabbit developmental studies. Meningocoele was observed in 2/261 (0.77%) rat foetuses at an oral dose of 120 mg/kg/d (main study) and in 12/291 (4.12%) foetuses at 240 mg/kg/d (range-finding study). In rabbits, at an oral dose of 100 mg/kg/d (main study), 1/48 foetuses (2.08%) had spina bifida and 1/48 foetuses had meningocoele, but no such abnormalities were detected at a dose of 200 mg/kg/d in a range-finding study conducted under identical conditions to the main study. It would seem reasonable to conclude that meningocoele appears to occur in a dose-related manner in rats, whilst there is less evidence for a clear effect of metham on abnormalities in rabbits. The doses at which these abnormalities occurred were around the threshold for maternotoxicity, and the effects would seem most likely to be related to the retardation of ossification of foetal skeletons (including those of the skull) associated with maternotoxicity. Such abnormalities were not observed in the developmental studies conducted with either MITC or dazomet, but the doses used in the studies for these two chemicals were lower than those used in the metham studies because of embryolethal effects. The highest doses of MITC used in the developmental studies were 25 mg/kg/d in rats and 10 mg/kg/d in rabbits, while the highest doses of dazomet were 30 mg/kg/d in rats and 75 mg/kg/d in rabbits (note that doses on a molar basis are still greater for metham; molecular weights for MITC, metham and dazomet are approximately 73, 107 and 162, respectively). A retardation of ossification of foetal skeletons was observed in the MITC studies, as well as the metham studies. It is unclear why metham appears to be less embryolethal than dazomet and MITC.

Metham-sodium was negative for genotoxicity, except in the human lymphocyte *in vitro* assay, where clastogenic effects were noted (both in the presence (20 - 40 µg/mL) and absence (20 µg/mL) of metabolic activation). It is noted that MITC also showed evidence of clastogenicity (in an *in vitro* chromosome aberration test in the Chinese hamster cell line V79).

DRAFT RECOMMENDATIONS

1. The lowest NOEL was 10 mg/kg/d po from the rat and rabbit developmental studies. The establishment of an ADI is not warranted given the lack of potential to form food residues.

2. The scheduling of metham sodium in schedule 6 would appear appropriate.

3. First Aid & Safety Directions**:**

   The current SDs for Metham are:

Metham-sodium	AC EC LD all strengths	120 130 131 132 133 161 162 163 164 180 210 211 220 222 279 280 285 290 292 294 299 300 303 330 332 340 342 350 360 361 364 365 366

   The avilable products are a soil fumigants (423 g/L), liquid soil fumigants (423 g/L), and foaming root fumigants (228 g/L). 423 g/L metham corrsponds to 510 g/L metham-sodium. On the basis that the active is the only ingredient which would contribute significantly to the toxicological profile of these products, and assuming a concentration of 510 g/L metham-sodium or less, the following SDs appear to be appropriate, based on hazard. It will be noted that there are no SDs related to PPE listed, as these will be supplied by Worksafe.

Amendments

   Metham-sodium AC EC LD all strengths - amend entry to read:

Metham-sodium	AE EC LD 510 g/L/kg or less	129 131 133 207 162 163 164 180 220 222 223 309 330 331 332 342 340 341 342 343 340 341 343 **... ... ... (**PPE from Worksafe)

   Prescription of SDs for metham-sodium in fumigant form needs to be considered further (hence 309?). It is noted that a conservative approach to eye irritancy has been taken and thus SDs for a severe eye irritation on the basis that although the eye irritation is said to be moderate for a 37% solution, the skin irritancy is severe in the same concentration. It seems somewhat unusual for a product to be less damaging to the eyes than to the skin.

   No change to the existing First Aid Instructions for metham-sodium is recommended.

4. WSA should consider by-stander exposure to gaseous MITC following the use of metham-sodium.

SUMMARY OF TOXICOLOGICAL HAZARD
(for TGAC, unless otherwise specified)

Date of Preparation:	May 1995
Chemical name:	Metham
Worst oral LD_{50} in rats:	450 mg/kg
Worst oral LD_{50} in other species:	50 mg/kg in mice
Worst dermal LD_{50}:	650 mg/kg in rats
Worst inhalation LC_{50}:	>4700 mg/m^3 in rats
Skin irritation:	severe in rats, rabbits (37% aqueous) slight in rats, rabbits (3% aqueous) technical material corrosive in rabbits
Eye irritation:	moderate in rabbits (3 and 37% aqueous)
Skin sensitisation:	moderate to strong in guinea pigs
Remarks:	Contact dermatitis observed in humans exposed to a 10% VAPAM (metham-sodium) solution
T-value:	20
NOEL:	10 mg/kg/d po in rat and rabbit developmental studies

Dazomet Summary

Evaluation of the mammalian toxicology and toxicokinetics of dazomet

SUMMARY

Introduction

Dazomet is a soil fumigant effective for the control of nematodes, insects, germinating weeds and soil fungi. Dazomet is strongly phytotoxic, acting by virtue of the chemical release of methylisothiocyanate (MITC). Dazomet is in schedule 6 of the SUSDP. The previous evaluator calculated an ADI of 0.005 mg/kg/d is based on a NOEL of 0.5 mg/kg (established in a 1-year dietary dog study and a 2-year dietary rat reproductive study) and a safety factor of 100. In the past, it has been considered questionable whether residues in food are an issue because dazomet breaks down in soil to MITC, which is highly volatile chemical. Also, MITC is phytotoxic, especially to young seedlings, and as the fumigant must be dissipated from the soil before a crop can be planted, no residues should appear in any crops. In the Australian MRL Standard, dazomet appears in Table 5 (Uses of substances where maximum residue limits are not necessary. Situations where residues do not or should not occur in foods or animal feeds;...). However, residue data submitted on dazomet for a variety of crops (submission number 7872), indicated that MITC may be a residue in crops following the use of dazomet.

Toxicokinetics and Metabolism

Results were provided on the absorption, distribution, metabolism and elimination in the rat following single oral dosing of [^{14}C]dazomet at levels of 10 and 100 mg/kg. One study was presented in full and the second study (which included the distribution data and involved dosing at the 10 mg/kg level) was presented in summary form only. [^{14}C]Dazomet was extensively absorbed from the GIT (>60% and possibly approaching 100%). Excretion was largely urinary, but a substantial amount of administered radiolabel was excreted in expired air. Analysis of portal vein plasma revealed very low concentrations of [^{14}C]dazomet, suggesting decomposition of dazomet during its passage across the gastrointestinal tract. Most of the radioactivity was detected as volatile compound, which was presumed (but not shown) to be MITC. Biliary excretion accounted for approximately 7% of radiolabel, while faecal excretion accounted for 2-3%, suggesting that enterohepatic recycling may occur. Following TLC analysis of radioactivity in urine, bile, liver and kidneys, a metabolic pathway was proposed. Repeated dosing did not alter the excretion or distribution of radioactivity. Tissue distribution studies revealed high concentrations of radioactivity in lungs, kidneys and liver, followed by ovaries, adrenals, thyroid and blood.

Acute Toxicity

Dazomet is of moderate acute oral toxicity. The oral LD_{50} values for dazomet from two different studies in rats were about 600 - 900 mg/kg for males and 400 - 550 mg/kg for females. The LD_{50} of dazomet, given subcutaneously to mice, was 248 mg/kg. The LD_{50} of dazomet, given subcutaneously to rats, was 470 and 550 mg/kg in males and females, respectively. The dermal LD_{50} of dazomet in rats was greater than 2000 mg/kg. Symptoms associated with acute dazomet toxicity were shaking, salivation, tonic convulsions, trembling, dyspnoea and lassitude.
In two studies, the introduction of 39 or 50 mg dazomet into the eye of rabbits caused slight irritation (moderate conjunctival erythema and slight oedema).

Results of two acute dermal irritation studies employing 50% aqueous preparations of dazomet in rabbits were reported. No irritation was observed in the study employing a 4 h exposure period. After a 20 h exposure period, moderate erythema and oedema were observed. Application of the EUP, Basamid Granular (2 g coated on a cottonwool carrier), to the rabbit ear for 20 h caused slight inflammation.

Skin sensitisation was not observed in two studies following the application of dazomet or Basamid Granular to the guinea pig. No justification was given for the doses/concentrations used in one of these studies and positive control compounds were not tested in these studies.

Short-Term Repeat-Dose Studies

In a range-finding study, rats were given dazomet in the diet at 0, 200, 800 and 3200 ppm for 3 weeks. Pronounced signs of toxicity (deteriorated general state, piloerection, squatting posture, paralysis of forelegs, pareses of hindlegs, strutting gait etc.) were seen only at the two highest doses. At 800 and 3200 ppm, food consumption was dramatically reduced, with reduced bodyweight gain or loss of bodyweight.

In a preliminary study, rats were given dazomet in the diet at 0, 20, 60, 180 and 540 ppm for 4 weeks. Clinical signs of toxicity (motor disturbances including pareses of hindlegs, strutting gait, abnormal foreleg position) were seen in high-dose females. There was reduced food consumption and bodyweight gain in high-dose females (also a trend in males) and also in 180 ppm females over the first 2 weeks. Several clinical chemistry changes were noted at 60 ppm and above. Liver weights were increased, accompanied by intermediary- and centro-acinary fatty degeneration in the form of large fat droplets (180 and 540 ppm males, 540 ppm females). There were no compound-related effects at 20 ppm.

A 21-day (6 h/d) inhalation study was carried out with rats. The inhalation of dazomet (33 g/m^3 of air) dust by rats did not result in any observable signs of toxicity.

Two 21-day dermal studies were conducted in rabbits. In the first study, the dermal application of dazomet in carmellose at doses of 10 and 100 mg/kg/d (6 h/d) to abraded skin resulted in well-defined erythema and oedema. Cutaneous hardening and discolouration resembling chemical burns were seen in 8/10 and 10/10 animals receiving, respectively, 0.5% (10 mg/kg/d) and 5.0% (100 mg/kg/d) dazomet to a 10 cm^2 area. In the second study, the dermal application of dazomet (5 days/week, 6 h/d to unabraded skin) at doses of 10, 100 and 1000 mg/kg/d did not result in any dermal irritation. There were no significant effects on clinical chemistry parameters, body weight, organ weights or macroscopic or microscopic findings. The NOEL in this study was 1000 mg/kg/d.

Subchronic Toxicity

In a mouse 10-week dietary range-finding study (summary only, provided), 800 and 1200 ppm dazomet in the diet for 71 days led to a slight reduction in bodyweight in high-dose males and, at both doses, reduced haemoglobin (Hb), red blood cell (RBC) counts, haematocrit (Hct) and (in females) reduced mean corpuscular haemoglobin concentration (MCHC), and increased MCH (mean corpuscular haemoglobin) and MCV (mean corpuscular volume).

In a 3-month study, mice were given 20, 60, 180, 360 and 540 ppm dazomet in the diet (summary only, provided). There were no clinical signs for any of the dose levels tested. At 360 and 540 ppm, haematological changes, similar to those seen in the 10-week mouse study, were observed (reduced Hb, RBC counts and MCHC, and in males, Hct, and increased MCV, reticulocytes, polychromasia and anisocytosis). There was also a slight increase in splenic haemosiderin deposition. An increase in absolute and relative liver weight was noted in males at 180 ppm and above and in high-dose females. On the basis of this finding, the NOEL was considered to be 60 ppm (estimated compound intake of 9 mg/kg/d).

In a 3-month study, rats were given dazomet in the diet at 0, 20, 60, 180 and 360 ppm. At the high dose, there was a slightly reduced bodyweight gain in both sexes. Some changes in serum chemistry were observed at 180 and 360 ppm and at the high dose there was a decrease in Hb levels. Increased liver weights were seen at 60 ppm and above, with fatty degeneration of liver cells (males only at 60 ppm). On the basis of this finding, the NOEL was 60 ppm (about 4.6 mg/kg/d) in females and 20 ppm (about 1.8 mg/kg/d) in males.

In a 3-month study, beagle dogs were given dazomet in the diet at 0, 25, 100 and 400/200 ppm. The high dose was reduced to 200 ppm on day 23 because of vomiting, inappetence and large losses in bodyweight at 400 ppm. At 200 ppm there was still reduced bodyweight gain. Hb, RBC counts and Hct values were reduced at the high dose and there were some changes in clinical chemistry parameters. Relative liver weights were increased in the 200 ppm animals and the 100 ppm males, without any histopathological correlates. There was a slight increase in splenic haemosiderin deposition at the high dose. The NOEL was 25 ppm (0.8-1.0 mg/kg/d) for males and 100 ppm (3.1-4.0 mg/kg/d) for females, on the basis of liver weight changes.

Chronic Studies

In a 78 week study, mice were given dazomet in the diet at 0, 20, 80 and 320 ppm. Compound intakes were estimated as follows: males - 0, 4, 16 and 68 mg/kg/d; females - 0, 6, 22 and 93 mg/kg/d. Survival was not affected and there were no noteworthy clinical signs, or bodyweight or food consumption changes. There was a significant elevation of liver weight at the high dose and an increased number of mid-dose and high-dose animals with liver discolouration, liver masses and centrilobular lipid deposition. At the high dose, females showed a slightly increased incidence of hepatocellular adenomas (3, 0, 1 and 7 females, out of 50, in the control, low dose, mid dose and high dose groups, respectively) and a significantly increased incidence of basophilic foci. Increased splenic haemosiderin deposition and extramedullary haematopoiesis were noted at the mid dose (males) and high dose. Three/60 females from each dose group had malignant lymphoma at one or more sites; because of the low incidence, lack of a dose-response, and lack of any effect in males, it was not considered to be directly compound-related. The NOEL was 20 ppm (about 4 mg/kg/d in males, 6 mg/kg/d in females).

Three 2-year rat studies were submitted. In the first, rats were given dazomet in the diet at 0, 5, 20, 80 and 320 ppm. Mean compound intakes were: males - 0, 0.3, 1, 4 and 18 mg/kg/d; females - 0, 0.3, 1, 6 and 23 mg/kg/d. Survival was not affected. At the high dose there was a reduction in bodyweight gain. Target organs were the liver and red blood cells (at the high dose in males and mid and high doses in females). Liver effects included increased relative weights, hepatocellular fat deposition, vacuolation, reduced plasma proteins and triglycerides, while red cell effects included reduced cell counts, Hb and Hct values. There was no evidence of any oncogenic effect of dazomet. The NOEL was 20 ppm (about 1 mg/kg/d) for females and 80 ppm (about 4 mg/kg/d) for males.

In the second 2-year study, rats were given dazomet in the diet at 0, 5, 20 and 80 pp. Mean compound intakes were: males - 0, 0.3, 1 and 4 mg/kg/d; females - 0, 0.3, 1 and 6 mg/kg/d. Survival was not affected and there were no clinical signs or effects on bodyweight gain and food intake. At the high dose, there was a slightly increased incidence of diffuse hepatocellular fat deposition and vacuolation, and in females, a slightly increased incidence of mixed cell and basophilic cell foci. There was no evidence of an oncogenic effect of dazomet. The NOEL was 20 ppm (about 1 mg/kg/d).

The third 2-year rat study was an old (1960) study. Rats were given dazomet in the diet at 0, 10, 40, 160 and 640 ppm. Mean compound intakes were: males - 0, 0.4, 1.7, 6.4 and 28 mg/kg/d; females - 0, 0.5, 2.0, 7.4 and 31.8 mg/kg/d. Survival was not affected. At the highest two doses there was a reduction in food consumption. Bodyweight was reduced at the 640 ppm dose and in females, also at the 160 ppm dose. Target organs were the liver and kidney. Liver and kidney weights were increased at the highest dose. The main lesions were glomerular nephritis in the kidney and focal necrosis in the liver. There was no evidence of an oncogenic effect of dazomet. There was no clear NOEL in this study, with effects being observed at all doses.

Dazomet was administered in the diet (0, 15, 50 and 150 ppm) to beagle dogs for 12 months. The high dose of 150 ppm (about 4.8 mg/kg) was hepatotoxic, resulting in increased liver weight, decreased albumin, chronic hepatitis, cirrhosis, hepatocellular hypertrophy, hepatocellular fatty change and increased pigment deposition in Kupffer cells. The latter was also observed in females at the mid dose. The NOEL was 50 ppm (about 1.6 mg/kg/d) for males, 15 ppm (about 0.5 mg/kg/d) for females.

Reproduction Studies

Dazomet was fed to rats at 0, 5, 30 and 180 ppm for at least 70 days prior to mating, throughout mating and lactation, during production of F_1a and F_1b litters. Selected F_1a pups were maintained on compound-containing diets post-weaning to produce F_2 litters. Hepatotoxicity was observed in both generations, mainly at the high dose, but to some extent at the mid dose. Liver weights were increased and there was an increased severity of liver fatty change. Some serum enzyme and serum protein changes also indicated effects on the liver. There was no impairment of mating or reproductive performance and no adverse effect on reproductive organs or pup development. The NOEL with respect to reproductive function in rats was 180 ppm (about 18 mg/kg/d), while that for systemic toxicity was 5 ppm (about 0.5 mg/kg/d).

Developmental Toxicity

An oral (gavage) developmental study was conducted in rats at dazomet doses of 0, 3, 10 and 30 mg/kg/d. Food intake and body weight and also uterine weights were reduced at the high dose and to a lesser extent at the mid dose. There was a higher incidence of runts at 10 mg/kg and above, however, without a clear dose-response relationship. There was no evidence of teratogenic effects. The NOEL for maternal and foetal effects was 3 mg/kg/d.

Two oral (gavage) developmental studies were carried out in rabbits. In the first study (0, 25, 50 or 75 mg/kg/d), clinical signs such as severe diarrhoea, apathy and unsteady gait, as well as depressed food consumption and body weight, were seen in does at 50 and 75 mg/kg/d. The number of live foetuses was greatly reduced (by 80%) at 50 and 75 mg/kg/d. This effect corresponded to a high number of dead implantations. There was no evidence of treatment-related foetal abnormalities, but low numbers of foetuses at 50 and 75 mg/kg/d made this difficult to assess. The NOEL for both maternal and embryo toxicity was 25 mg/kg/d.
In the second study (0, 6.25, 12.50 or 25.00 mg/kg/d), embryotoxicity, expressed as increased dead implantations, in particular, increased early resorptions, resulting in reduced numbers of live foetuses, was seen at 25 mg/kg/d. There was no evidence of a teratogenic effect of dazomet. Maternal toxicity was not observed in this study (NOEL > 25 mg/kg/d). The NOEL for embryotoxicity was 12.5 mg/kg/d.

Genotoxicity Studies

A wide range of genotoxicity studies were conducted on dazomet including both *in vitro* and *in vivo* tests and covering gene mutation, chromosome effects and DNA damage assays. Some of these studies gave weakly positive results and some gave negative results.

Results from Ames tests were reported by five different groups. Tests were done using *S. typhimurium*, and in one case, also *E. coli WP2 hcr*; four of the studies were done both in the presence and absence of metabolic activation. None of these studies was positive, nor was a test using *Saccharomyces cerevisiae.* Negative results were also obtained in a host-mediated assay using mice and *S. typhimurium* G46. In contrast, in a gene mutation assay at the HGPRT locus in Chinese hamster ovary cells, dazomet induced small increases in mutation rate, both in the presence and absence of metabolic activation, although this increase did not appear to be concentration dependent in the presence of metabolic activation. A forward mutation assay at the TK locus in L5178Y mouse lymphoma cells produced equivocal results. In this assay, dazomet did not increase the mutation frequency when tested in the presence of metabolic activation, but in the absence of metabolic activation, an increase in mutation frequency (in the order of 2- to 3-fold) was observed in 2 out of 3 tests, but these increases were not concentration dependent.

Six chromosome effects assays were conducted, three *in vitro* and three *in vivo.* Dazomet was negative in four of these assays: a mouse micronucleus assay and chromosome aberration assays in human lymphocytes *in vitro,* and in rat bone marrow cells and Chinese hamster spermatogonia after dosing *in vivo.* In contrast, dazomet was positive in two assays, both being chromosome aberration assays in mouse lymphoma L5178Y cells *in vitro,* but these assays were conducted by two different laboratories. In one study (Stauffer Chemical Company), positive results were only observed in the absence of metabolic activation. However, reproducible, concentration-dependent increases in both structural and numerical aberrations were observed in two separate experiments by this laboratory. Endoreduplication, a rare numerical aberration, was observed at most concentrations of dazomet and translocations, triradials and quadriradial, which are rare structural aberrations, were observed at some concentrations. In the other study (Litton Bionetics, Inc.), significant increases in the numbers of cells with aberrations were observed both in the presence and absence of metabolic activation, but they were not clearly concentration dependent. However, again, some rare structural aberrations were observed (mainly in the absence of metabolic activation).

Dazomet was not found to be genotoxic in two *B. subtilis* rec assays which were both conducted in the presence and absence of metabolic activation.

Two laboratories conducted studies of the potential of dazomet for inducing SCEs. One study produced negative results (Stauffer Chemical Company). In the other study (Litton Bionetics, Inc.), in the absence of metabolic activation, there was a small, but significant, increase in the number of SCEs/chromosome at the highest concentration tested.

Two laboratories conducted studies of the potential of dazomet to induce unscheduled DNA synthesis in rat primary hepatocytes. One study (Hazleton Biotechnologies Company) was conducted with dosing *in vivo*, whereas the other study (Litton Bionetics, Inc.) was conducted *in vitro.* The *in vivo* study was negative, but positive results (weak, but reproducible increases in nuclear labelling) were obtained in the *in vitro* study.

Two laboratories conducted studies of the potential of dazomet to induce cell transformation in BALB/c-3T3 cells. In neither study did dazomet induce transformation.

Human Studies
A published article described case reports of contact dermatitis arising from exposure to dazomet.

DISCUSSION

The data package for dazomet is reasonably extensive, covering information on the impurities in the TGAC and data on metabolism (summary form only) and subchronic, chronic, reproductive and developmental toxicity.

Dazomet is degraded in the soil to MITC (a highly volatile chemical), which appears to be a chemical rather than a biological process. Because of this instability, and also the phytotoxicity of MITC, it is questionable whether exposure of the human population to dazomet (or MITC) via food residues is an issue. It would appear that following oral ingestion (at least in the rat), dazomet is rapidly degraded to MITC during its passage across the intestinal tract. It is not known to what extent dazomet is metabolised to MITC by the skin or lung epithelium.

High dietary doses of dazomet appeared to cause nervous system effects. Thus, doses of 540 to 800 ppm and above (in 3- and 4-week studies) in rats caused strutting gait, foreleg paralysis, and paresis of hindlegs in rats. Doses of 80 and 320 mg/kg in dogs caused high-stepping gait and forelimb weakness.

Dazomet has moderate to low acute oral, dermal and inhalational toxicity. It appears that the toxicity of dazomet is somewhat greater by the oral route than by the dermal and inhalational routes. Dazomet is only a slight dermal and ocular irritant. This is in contrast to MITC which is a severe local irritant. Unlike MITC, dazomet did not cause stomach lesions, which is probably a reflection of its lower local irritancy than that of MITC (dazomet at least must pass across the gut wall before it is metabolised to MITC, therefore following oral dosing with dazomet, all organs/tissues are exposed to MITC except the stomach mucosa). Nevertheless, dazomet might exert eye, skin and lung irritancy following conversion to MITC and volatilisation of the latter. Furthermore, systemic exposure to MITC might possibly occur, via the inhalational or dermal routes, following the use of dazomet.

Skin sensitisation tests in guinea pigs were negative, but it is not clear to what extent this may reflect inadequacy of the doses/concentrations tested/experimental conditions.

Haematological effects (predominately on red blood cells) were major toxicological effects of dazomet. Red blood cells appeared to be a target organ. Thus, in mice (10-week and 3-month dietary studies) and dogs (3-month dietary study) there was a reduction in red cell parameters (Hb, RBC count and Hct), with polychromasia and anisocytosis observed in the 10-week mouse study. These findings were accompanied by increases in splenic haemosiderin deposition. Also, extramedullary haematopoiesis was noted in a 78-week dietary mouse study, while deposition of iron-positive pigment was noted in the liver of dogs in a 1-year dietary study. It is unclear why the red blood cells appear to be a target of dazomet but not of MITC, although it is possible that this observation can be explained by the higher doses used in the dazomet studies than the MITC studies (which were possible to achieve because of the lower local irritancy of dazomet than MITC).

Another target organ for toxicity was the liver (which was also a target organ of MITC). Increases in absolute and relative liver weights were consistently seen in repeat-dose studies in mice, rats and dogs. For these three species the three-month studies gave the lowest doses (dietary) at which increased liver weights were observed and these doses were 180 and 540 ppm in male and female mice, respectively, 60 and 180 ppm for male and female rats and 100 and 200 ppm for male and female dogs. Fatty degeneration of hepatocytes, vacuolation and liver discolouration (rats), centrilobular lipid deposition (rats and mice), reduced total protein and albumin (rats and dogs), moderate-severe chronic hepatitis and cirrhosis (dogs) were also observed after long-term administration of dazomet. Hepatotoxicity was more marked in the dazomet studies than in the MITC studies, which is probably due to the higher doses used in the dazomet studies than the MITC studies.

In one of the two-year rat studies, there was also evidence for the kidney as the target organ, with the main lesion resembling glomerular nephritis.

Rat studies showed no clear evidence of any carcinogenic effect of dazomet. In mice, there was a slight increase in hepatocellular adenomas (not carcinomas) following 78 weeks of treatment at the high dose (320 ppm). There was also an increase in malignant lymphoma in females, but because of the low incidence, the lack of effect in males and the lack of any dose-response, it was not considered to be directly compound-related. The lack of a carcinogenic effect of dazomet is consistent with the data for MITC.

The lowest NOEL of about 0.5 mg/kg was established in a 1-year dietary dog study and in a 2-generation dietary rat reproductive toxicity study. This NOEL was based on deposition of iron-positive pigment in the livers of female dogs at the next highest dose (50 ppm or approx. 1.6 mg/kg/d). In rats, the lowest NOEL determined was in the 2-generation reproductive toxicity study, and was based upon reduced bodyweight gains and increased incidence and severity of liver fatty changes at the next highest dose (30 ppm, or about 3 mg/kg/d). However, in one of the 2-year chronic toxicity studies, an NOEL was not determined, with increases being observed in the incidence of histological lesions in the liver and the kidney at the lowest dose tested (40 ppm, ie. 0.4 - 0.5 mg/kg/d). The LOEL in the Mellon 2-year rat study (0.5 mg/kg/d) was the same as the NOEL from the dog study on which the current ADI is based.

Dazomet was not teratogenic at oral doses of up to 30 mg/kg in the rat and at oral doses of up to 25, 50 or 75 mg/kg in the rabbit (although at the latter two doses, there were not a large number of live foetuses for examination). This lack of evidence of a teratogenic effect of dazomet is consistent with the data for MITC.

An acceptable package of mutagenicity tests has been conducted covering all three end points. The results are the genotoxicity tests are not clear cut. While the majority of tests gave negative results, there were sufficient positive results to indicate some genotoxic potential of dazomet.

In summary, there were positive results in one gene mutation assay (HGPRT locus in Chinese hamster ovary cells), equivocal results in another gene mutation assay (TK locus in mouse lymphoma L5178Y cells), and positive results in two chromosome aberration assays (both *in vitro* assays in mouse lymphoma L5178Y cells), in one *in vitro* assay for of unscheduled DNA synthesis in primary rat hepatocytes and in one *in vitro* assay of sister chromatid exchange. In all cases, the positive findings were relatively weak. There were no positive *in vivo* studies and there was a trend for results to only be positive (or to be stronger) in the absence of metabolic activation than in its presence. This suggests that unchanged dazomet has greater genotoxic potential than the metabolites of dazomet. The unscheduled DNA synthesis assay was the only assay which gave results suggesting that the metabolites of dazomet may have some genotoxic potential, even if only weak.

Although exposure of the human population to dazomet via food residues appears to be unlikely, an ADI has been previously set at 0.005 mg/kg/d based on the NOEL of 0.5 mg/kg/d from the dog study and using a safety factor of 100. Given the lack of determination of an NOEL in the Mellon 2-year rat study, and the evidence that dazomet (at least in the unchanged form) has some genotoxic potential, it would be appropriate to increase the safety factor from 100 to 1000, and correspondingly revise the NOEL down by a factor of 10.

DRAFT RECOMMENDATIONS

1. The scheduling of dazomet in the SUSDP at schedule 6 is considered appropriate on toxicological grounds.

2. ADI

   The ADI for dazomet should be reviewed in light of the data from the 2-year chronic study in Carworth-Wistar rats (Mellon Institute of Industrial Research, University of Pittsburgh). No NOEL was determined in this study (ie. the NOEL was lower than the lowest dose tested). It is recommended that the ADI is 0.0005 based on the LOEL in the above study of 0.5 mg/kg/d and a safety factor of 1000.

   The National Registration Authority should review the residue data in light of the information suggesting that MITC may be a residue in crops following the use of dazomet.

3. First Aid and Safety Directions

   Dazomet EUP is Basamid Granular which is a 97% formulation of dazomet, comprising granules. The only excipient listed is 0.1% silica gel. Use pattern is as a soil fumigant which is applied directly to the soil in granular form.

   Current Safety Directions are:

Dazomet	GR 980 g/kg or less	120 130 133 161 162 163 164 210 211 220 221 279 283 290 294 297 320 340 342 350 360 361 363 366

   Given the acute toxicological profile of dazomet, there is no evidence to suggest that a change to the existing safety directions, based on hazard, is required. Worksafe Australia may wish to review the safety directions relating to PPE.

   No change to the existing First Aid Instructions for dazomet is recommended.

4. WSA may wish to consider by-stander exposure to gaseous MITC following the use of dazomet.

SUMMARY OF TOXICOLOGICAL HAZARD*

Date of Preparation:	July 1996
Chemical name:	Dazomet
Worst oral LD_{50} in rats:	415 mg/kg (females)
Worst oral LD_{50} in other species:	Not available
Worst dermal LD_{50}:	> 2000 mg/kg in rats
Worst inhalation LD_{50}:	8400 mg/m^3 in rats
Skin irritation:	Slight in rabbits
Eye irritation:	Slight in rabbits
Skin sensitisation:	Nil in guinea pigs at the doses tested
Remarks:	Contact dermatitis reported in humans
T-value:	40

NOEL: An NOEL was not determined in a chronic (2-year) dietary study in rats (Mellon Institute of Industrial Research, University of Pittsburgh). At the lowest dose tested (10 ppm, corresponding to about 0.5 mg/kg/d), there was an increase in the incidence of kidney and liver lesions. The lowest established NOEL was 0.5 mg/kg/d, in a 1-year dietary dog study and a 2-generation dietary rat reproductive toxicity study.

* This summary largely refers to the TGAC, but it would be expected that there would be little difference between the toxicity of the TGAC and EUP, given that the difference between the two forms is only one of particle size (larger for Basamid Granular than for the TGAC).

Methylsiothiocyanate Summary

Evaluation of the mammalian toxicology and toxicokinetics of Methylisothiocyanate (MITC)

SUMMARY

Introduction

Methylisothiocyanate (MITC) is a pre-plant soil fumigant for control of nematodes, soil fungi and insects. It is a relatively volatile compound, which therefore evaporates from the soil into the air. It is currently in schedule 6 of the SUSDP. No ADI has been set. It is not currently registered in Australia because the application was withdrawn by the company and has never been considered by the PACC or PACSC.

Metabolism and Toxicokinetics

Evidence was presented that orally administered MITC is excreted in rats as a mercapturic acid conjugate. This is likely to proceed via glutathione, cysteinylglycine and cysteine conjugates. Excretion in the rat was largely urinary and no unchanged MITC was present in 24 h urine. A tissue distribution study revealed highest concentrations of radioactivity in the thyroid and pituitary at 7 d postdose. The available data in rats suggest that MITC is likely to be completely metabolised to single carbon compounds which are incorporated into the general metabolic pool.

Urine was also the major route of excretion in the dog, but a large proportion of administered radioactivity (about 20%) remained in the tissues at 7 d postdose, with liver and thyroid having the highest concentrations. Urinary metabolic profile differed considerably between rats and dogs.

Acute Toxicity

MITC is a moderately toxic compound. The oral LD_{50} is 72 mg/kg in rats and 90 mg/kg in mice. The acute oral NOEL in dogs is approximately 0.1 mg/kg based on necropsy findings at 0.5 mg/kg. In monkeys, the acute oral NOEL was < 10 mg/kg. In rabbits, the acute oral NOEL was > 10 mg/kg. Haemorrhagic lesions were observed in the stomach in monkeys and dogs. The dermal LD_{50} was 1870 mg/kg in mice, approximately 1000 mg/kg in rats and 33 mg/kg in rabbits. Inhalation LC_{50} was 540 mg/m^3 in rats (4 h exposure).

MITC was shown to be a severe eye and skin irritant in rabbits. In maximization tests in guinea pigs, MITC showed weak skin sensitising potential.

Short Term Repeat Dose Studies

No NOEL was demonstrated for skin effects after repeated daily application of MITC to rats for 1 month. The lowest dose tested was 1 mg/kg/d. Erosion/necrosis of the skin was observed at doses of 100 mg/kg and above.

Subchronic Toxicity

Several subchronic (3 month) gavage studies have been conducted at doses up to 20 mg/kg/d in mice, 40 mg/kg/d in rats and 2 mg/kg/day in dogs. In rats and mice, corrosive effects on the stomach were observed. In all species tested, changes were observed in the liver, in particular fatty changes. "Spermatogenic disorder" was observed in rats and mice and a decrease in testes weight in dogs. In some studies a NOEL could not be demonstrated. The NOEL in the mice (gavage) study was 0.7 mg/kg based on increased liver weight at 1 mg/kg/d. The NOEL in the dog (gavage) study was 0.04 mg/kg/d based on decreased testes weight and increased liver effects at 0.4 mg/kg/d.

In a 3 month inhalation study (nose only 4 h/d) the NOEL was 10 ppm (30.7 mg/m^3) based on clinical signs (apathy, salivation and nasal discharge) observed at 45 ppm.

Chronic Toxicity

Chronic (2 year) studies with MITC administered in drinking water have been conducted in mice and rats. There was no carcinogenic effect observed in either species. The major toxicological findings were decreased body weight gain and decreased food or water intake. The NOEL for the mice study was 20 ppm (3.48 mg/kg/d) in drinking water (the next highest dose being 80 ppm) and the NOEL for the rat study was 10 ppm (0.5 mg/kg/d) in drinking water (the next highest dose being 50 ppm).

Reproductive Toxicity

In a three-generation oral reproduction study, rats were dosed at 0, 1, 3 and 10 mg/kg (5 d/week) beginning at 28 d of age in all generations. Histopathological examination revealed increases in the incidences and severity of mucosal acanthosis and hyperkeratosis in the forestomach (non-glandular portion of the stomach) of treated animals (F_0, F_1 and F_2 generations). Parameters of reproductive performance and the incidences of gross fetal abnormalities were not altered by treatment for any generation. No NOEL was observed in this study because the forestomach lesions occurred at all dose levels (ie. NOEL < 1 mg/kg/d).

Developmental Toxicity

Two gavage teratology studies were conducted in rats. Doses of MITC that did not cause maternal toxicity were not associated with fetal toxicity, nor teratogenicity. In the first study, at the highest dose tested (25 mg/kg/d) there was fetal growth retardation, presumably secondary to decreased maternal weight gain and decreased maternal food intake. The NOEL was 5 mg/kg, based on decreased fetal size at 25 mg/kg/d. In the second study, there was an increase in the number of runts at the high dose (30 mg/kg/d), presumably secondary to decreased maternal weight gain. NOEL for embryo/foetotoxicity in this study was 10 mg/kg/d. There was no clear NOEL for maternotoxicity because of a reduction in "corrected" body weight at all doses tested.

Three oral teratology studies were conducted in rabbits. In the first study (0, 1, 3 and 10 mg/kg/d), there was high mortality of does at the high dose and body weight was deleteriously affected at the mid and high doses. At the high dose, there was an increase in the number of resorptions and a decrease in the number of live pups at birth, in pup birth weight and in 24-h pup viability. There was a dose-related increase in the percent of fetuses with incompletely ossified sternum sections. NOEL for maternal toxicity was considered to be 1 mg/kg/d, while that for fetal toxicity was 3 mg/kg/d (if the increase in the percent of fetuses with incompletely ossified sternum sections is not considered, otherwise no NOEL was determined for fetal toxicity).

In the second study (doses of 0, 1, 3 and 5 mg/kg/d), numbers of fetuses were higher in the test groups than in the control group and there was a significant reduction in weight and length of high-dose fetuses . There was a increased incidence of minor anomalies of the heart or major blood vessels in high-dose fetuses , probably due to fetal growth retardation, and although the total incidence of fetuses with skeletal variants was comparable for all groups, there was an increase in the incidence of fetuses with an extra pair of ribs in the high-dose fetuses . The NOEL for both maternal and fetal toxicity was considered to be 5 mg/kg/d.

In the third study (doses of 0, 1, 3 and 10 mg/kg/d), there were no effects on the fetuses . Thus the NOEL for embryo/fetotoxicity was 10 mg/kg/d. The NOEL for maternotoxicity was 3 mg/kg/d because of a reduced body weight gain over the treatment period in the high-dose does.

Genotoxicity

MITC was tested in the Ames test in a number of laboratories: Inveresk Research Laboratories, Schering laboratories, BASF Laboratories, Germany and the Institute of Environmental Toxicology, Tokyo. All studies were conducted both in the presence and absence of metabolic activation and used 4 or 5 strains of *S. typhimurium*, and the latter additionally used an *E. coli* strain. MITC was tested at up to toxic concentrations in all studies. There was no evidence of a mutagenic potential of MITC in any of these studies or in a test for gene mutation at the HGPRT locus in Chinese hamster V79 cells.

MITC was negative in two rec assays using *B. subtilis*, and it did not induce unscheduled DNA synthesis in an assay in primary rat hepatocytes.

Whilst MITC did not show evidence of a chromosome damaging effect in an *in vivo* mouse micronucleus test employing an oral dose at the LD_{10}, or in an *in vitro* chromosome aberration test in human lymphocytes, it was positive in an *in vitro* chromosome aberration test in Chinese hamster V79 cells. In the *in vitro* test, MITC induced an increase in the percentage of aberrant cells (both including and excluding gaps), and caused nuclear disintegration, both in the presence and absence of metabolic activation at a harvest conducted at 28 h after the start of treatment. A large proportion of the aberrations induced were chromosome breaks and chromosome exchanges. Minimal or no increases were seen at the other harvest times (6 h and 12 h).

DISCUSSION

MITC (technical) is severely corrosive to tissues and is thus a severe eye and skin irritant. Corrosive effects on the stomach were observed in rats, mice, dogs and monkeys following oral dosing. MITC was shown to have skin sensitisation potential. MITC is of moderate acute toxicity via the oral, dermal and inhalational routes. High doses of MITC appeared to cause some nervous system effects such as convulsions, piloerection and changes in posture.

The liver is a target organ and to a lesser extent, the testes. Thus, in 3-month oral mouse studies, increased liver weights were observed at doses of 0.7 mg/kg and above and fatty degeneration of the liver was observed at 20 mg/kg. In a 3-month oral dog study, there was an increase in the incidence and severity of periportal hepatocyte vacuolation and lipid deposition at 0.4 and 2 mg/kg. "Spermatogenic disorder" was observed in a 3-month oral study in mice at a dose of 20 mg/kg, but not at 5 mg/kg, and in a 3-month oral rat study at 40 mg/kg (10/10 animals affected) and at 10 mg/kg (1/10). There was no evidence of an effect on reproductive performance in rats, but the reproductive study only employed doses (oral) of up to 10 mg/kg (stomach, but not liver or testicular lesions were observed in this study).

MITC was not carcinogenic in mice at doses of up to about 27 mg/kg/d in the drinking water for 2 years, nor in rats at doses of up to 1.6 (females) or 2.7 mg/kg/d (males). The major toxicological findings in the chronic studies were decreased body weight and decreased food or water consumption. Hepatotoxicity and testicular toxicity were not observed in the 2-year mouse study, possibly due to a different strain being used compared to that in the 3-month study. No histopathological effects were observed in the 2-year rat study, probably because of the relatively low doses used. MITC was not teratogenic at oral doses of up to 25 mg/kg in the rat and at oral doses of up to 10 mg/kg in the rabbit.

There were adequate data to establish an NOEL. The dog appears to be the most sensitive species. The lowest NOEL of about 0.04 mg/kg/d was established in a 3-month dog study (gavage). This was based on decreased testes weight and increased liver effects at 0.4 mg/kg/d. In the 2-year rat study (compound administered via drinking water), an NOEL of about 0.5 mg/kg/d was established based on decreased body weight gain at the next highest dose.

There was no evidence of a mutagenic effect of MITC in a number of tests covering the major end-points. These testes included Ames tests (*S. typhimurium* and *E. coli*), a test for gene mutation at the HGPRT locus, a test for chromosome aberrrations in human lymphocytes *in vitro* and tests for DNA damage (rec assays in *B. subtilis* and unscheduled DNA synthesis assay in primary rat hepatocytes). MITC was negative in an *in vivo* clastogenicity test (mouse micronucleus test), but was clearly positive in an *in vitro* clastogenicity test (chromosome aberration test in Chinese hamster V79 cells) at one time point, but not at other time points. MITC could be considered to have equivocal clastogenic potential.

DRAFT RECOMMENDATIONS

1. Whilst a considerable number of additional studies have been reviewed in this evaluation, no change in the previously established NOEL is required. The lowest NOEL is 0.04 mg/kg/d based on decreased testes weights and liver effects seen in the 3 month gavage study in dogs.

2. The scheduling of MITC in schedule 6 is appropriate on toxicological grounds.

3. The existing SDs for MITC are:

Methyl isothiocyanate	All strengths	130 131 132 133 206 162 161 163 164 210 211 220 222 230 279 280 283 290 292 294 298 301 330 331 332 342 340 341 342 343 340 341 343 370

Information on formulations and use pattern/application methods for each product are usually used in developing SDs. However, given that MITC is not marketed in Australia, such information is not availableand so SDs, if prescribed, would have to be based on the 96% TGAC. Given the toxicological profile of technical MITC, the following SDs, based on hazard, may be appropriate (Worksafe would prescribe SDs related to PPE):

Amendments

Methy isothiocyanate - amend entry to read:

Methyl isothiocyanate	All strengths	100 130 131 132 133 205 206 162 220 222 223 230 207 164 340 343 330 332 340 342 **... ...** PPE from Worksafe)

No change to the existing First Aid Instructions for MITC is recommended.

4. WSA should consider by-stander exposure to gaseous MITC.

SUMMARY OF TOXICOLOGICAL HAZARD (TGAC)

Date of preparation:	July 1996
Chemical name:	Methylisothiocyanate
Worst oral LD_{50} in rats:	72 mg/kg
Worst oral LD_{50} in other species:	90 mg/kg in mice
Worst dermal LD_{50}:	33 mg/kg in rabbits
Worst inhalation LC_{50}:	540 mg/m^3 in rats
Skin irritation:	severe in rabbits
Eye irritation:	corrosive in rabbits
Skin sensitisation:	weak skin sensitisation in guinea pigs
Remarks:	
T-value:	7
NOEL:	The lowest NOEL was 0.04 mg/kg/d, based on decreased testes weights and liver effects seen in a 3-month gavage study in dogs.

Comparative Review of Metham-Sodium, Dazomet and MITC

1. INTRODUCTION

Metham (and its sodium salt, metham-sodium) is a dithiocarbamate soil fumigant with fungicide, nematocide, herbicide and insecticide activity. There are several end use products (EUP) containing metham-sodium registered in Australia for use in a range of crops, including ornamentals, food and fibre crops and tobacco. Some of the EUPs are used as inhibitors of root growth in sewer lines.

Metham-sodium was placed on the National Registration Authority's Special Review Program after consideration at the 17th meeting of the Interagency Co-ordination Committee (ICC). This was following receipt of correspondence from an orchardist from Shepparton, Victoria, who experienced severe eye irritation and nausea when applying metham-sodium to fumigate a small nursery site. The safety directions are to be reviewed following review of toxicology data by this Department. It is noted that complaints following the use of metham-sodium have been made previously and in August, 1991, the then DPSSC considered information provided by Victoria on the irrigation use of metham, the former Advisory Committee on Agricultural Chemicals (ACAC) consideration of its use and comments from the municipal council involved with the complaint. The committee considered that spraying, irrigation and flood irrigation were not appropriate application methods and ACAC agreed in principle with this.

The method of application of the end use product, VAPAM, by the Victorian fruitgrower whose correspondence initiated the review was by hand held boom from a motorised spray unit. The spray was then incorporated into the soil by a tractor mounted rotary hoe and the soil was sealed with black plastic.

This review of the acute toxicity and safety directions for metham-sodium has been extended to a consideration the related compounds, dazomet and methylisothiocyanate (MITC). Both metham-sodium and dazomet rapidly decompose in soil to MITC. This decomposition is a chemical rather than a biological process. However, it is likely that the toxicological profile of metham-sodium and dazomet result from the formation of MITC. A listing of EUPs for metham-sodium and dazomet are attached. MITC is not registered in Australia.

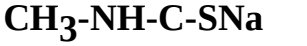
Currently, metham is in Schedule 6 of the SUSDP, as are dazomet and MITC. No ADI has been set for MITC or metham, but an ADI of 0.005 mg/kg/d for dazomet has been established. The ADI was based on an NOEL of 0.5 mg/kg (established in a 1-year dietary dog study and a 2-year dietary rat reproductive study) and a safety factor of 100. Recent data on dazomet has resulted in a proposed amendment for the ADI to 0.0005 mg/kg/day based on the LOEL of 0.5 mg/kg/day in a chronic 2 year rat study and using a 1000 fold safety factor.

The Department has undertaken an extensive review of the toxicity of metham, dazomet and MITC, including evaluation of previously unevaluated data and consolidation of previous toxicology reports. The following overview consolidates all available acute toxicological data which have been submitted for metham-sodium, dazomet and MITC. For full details of these data, the individual assessment reports for each chemical are attached.

Chemical Structures

MITC

Metham-sodium
(anhydrous)



Dazomet

2. ACUTE TOXICITY

Lethal dose Studies

The acute lethal dose data for technical MITC, technical dazomet and technical metham-sodium, via various routes of administration, are summarised in Table 1 below.

Table 1: Summary of acute lethality of technical MITC, technical metham- sodium and technical dazomet.

SPECIES	STRAIN	SEX	MITC	DAZOMET	METHAM
Acute Oral LD50 (mg/kg)					
Rat	Sprague	M	220	596	
Rat	Sprague	F		415	
Rat	?				450 (M/F); 820 (M/F); 1800 (M)/1700 (F); 1294 (M)/1428 (F)
Rat	Donryu	M	175		
Rat	Donryu	F	72		
Rat	Wistar	M/F	95		
Rat	Wistar	M	about 163		
Rat	Wistar	F	about 147		
Mouse	dd	M	90		
Mouse	CF-1	M	110		
Mouse	dd	F	104		
Mouse	?	M/F			47; 50; 285
Mouse	NMRI/WIGA	M	about 120		
Mouse	NMRI/WIGA	F	about 100		
Rabbit	?	M/F			320
Cat	?	M/F			100
Guinea Pig	?	M/F			815

Table 1 (cont.)

SPECIES	STRAIN	SEX	MITC	DAZOMET	METHAM
Dermal LD50 (mg/kg)					
Rat	Donryu	M	2780		
Rat	Wistar	M	about 1000		
Rat	Wistar	F	1930		
Rat	Sprague	M/F		>2000	
Rat	?	M/F			647
Mouse	dd	M	1870		
Rabbit	NZ White	F	33		
Rabbit	NZ White	M/F	263		
Rabbit	?	M/F			800; 1012; 1300
Subcutaneous LD50 (mg/kg)					
Rat	Donryu	M	60		
Rat	Donryu	F	59		
Rat	Wistar	M		470	
Rat	Wistar	F		550	
Mouse	dd	M	75		
Mouse	dd	F	89		
Mouse	ICR	M/F	-	248	
Intraperitoneal LD50 (mg/kg)					
Rat	Donryu	M	54		
Rat	Donryu	F	56		
Mouse	dd	M	82		
Mouse	dd	F	89		
Mouse	NMRI	M/F		~280	
Inhalational LC50 (mg/m^3)					
Rat	CFY	M/F	1900		
Rat	Sprague, CD	M/F	540		
Rat	Wistar	M		>8400	
Rat	Wistar	F		7290	
Rat	?	M/F			>4700

MITC is a moderately toxic compound. The oral LD_{50} is 72 mg/kg in rats and 90 mg/kg in mice. The acute oral NOEL in dogs is approximately 0.1 mg/kg based on necropsy findings at 0.5 mg/kg. In monkeys, the acute oral NOEL was < 10 mg/kg. In rabbits, the acute oral NOEL was > 10 mg/kg. Haemorrhagic lesions were observed in the stomach in monkeys and dogs. The dermal LD_{50} was 1870 mg/kg in mice, approximately 1000 mg/kg in rats and 33 mg/kg in rabbits. Inhalation LC_{50} was 540 mg/m^3 in rats (4 h exposure).

Metham-sodium has moderate acute oral and dermal toxicity, with lowest oral LD_{50} values of 50 mg/kg (mouse), 100 mg/kg (cat), and 450 mg/kg (rat), and lowest dermal LD50 values of 650 mg/kg (rat) and 800 mg/kg (rabbit). Acute inhalation toxicity was low in rats with an LC_{50} >4700 mg/m^3.

The oral LD50 values for dazomet from two different studies in rats were about 600 - 900 mg/kg for males and 400 - 550 mg/kg for females. The oral LD_{50} of dazomet, given subcutaneously to mice, was 248 mg/kg. The LD_{50} of dazomet, given subcutaneously to rats, was 470 and 550 mg/kg in males and females, respectively. The dermal LD_{50} of dazomet in rats was greater than 2000 mg/kg. Symptoms associated with dazomet toxicity were shaking, salivation, tonic convulsions, trembling, dyspnoea and lassitude.

Acute lethal dose toxicity findings for formulations are somewhat limited for these chemicals, but data on liquid MITC (VORLEX 77) indicate that the oral LD_{50} in rat was 0.18 mL/kg, the inhalational LD_{50} in rat was 5600 mg/kg, the rabbit dermal LD_{50} was 0.09 mL/m^3 and the ip LD_{50} in rat was 0.15 mL/mg. Basamid had an oral LD_{50} of about 640 mg/kg in rats and an ip LD_{50} of about 280 mg/kg in mice.

Irritation Studies

The eye and dermal irritation and skin sensitisation potential of MITC, dazomet and metham-sodium, both technical and formulation, are summarised in Table 2 below. Details of these findings are also discussed below.

Table 2: Summary of eye irritation, dermal irritation and skin sensitisation potential of MITC, dazomet and metham (technical and/or EUP).

TGAC/EUP	MITC	METHAM	DAZOMET
Eye Irritation in Rabbit			
TGAC	very severe	irritant	slight
EUP		mild-moderate (3%, 37% and 50% aq)	slight
Dermal Irritation in Rabbit			
TGAC	severe	corrosive (50%suspens.)	nil
EUP		slight to severe* (3%, 37% and 50% aq)	slight
Skin Sensitisation Potential in Guinea Pig			
TGAC	weak		none
EUP	weak	moderate-strong	none

* findings also in rat

MITC was shown to be a severe eye and skin irritant in rabbits. Technical grade MITC and MITC formulated as TRAPEX 40 had weak skin sensitising potential in maximization tests in guinea pigs.

Metham-sodium (37% aqueous solution) produced severe skin irritation in rats and rabbits and the technical material was corrosive to rabbit skin. As a 3% aqueous solution, metham-sodium produced slight skin irritation in rats and rabbits. Metham-sodium (as a 3% or 37% aqueous solution) was a moderate eye irritant in rabbits. It was a moderate to strong skin sensitiser in guinea pigs.

The introduction of 39 or 50 mg dazomet into the eye of rabbits caused slight irritation (moderate conjunctival erythema and slight oedema). Results of two acute dermal irritation studies employing 50% aqueous preparations of dazomet in rabbits were reported. No irritation was observed in the study employing a 4 h exposure period. After a 20 h exposure period, moderate erythema and oedema were observed. Application of Basamid Granular (2 g coated on a cottonwool carrier) to the rabbit ear for 20 h caused slight inflammation. Skin sensitisation was not observed in either of two studies following the application of dazomet to the guinea pig, but there was no justification of the doses/concentrations used in these studies.

3. HUMAN STUDIES

From observations on nine patients with occupational dermatitis from MITC, it was concluded that MITC causes primarily a toxic dermatitis, but induces sensitisation as well. Although all the patients had contact with the soil disinfectants (dazomet or metham-sodium) for a few days or less, 8 of the 9 patients showed positive patch test reactions to VAPAM (metham-sodium) at a non-irritant concentration of 0.05% in water, and the results could be elicited 1 year later.

In a published paper, 15 cases of contact dermatitis were reported in an unspecified number of workers in potato production occupations following the use of a 10% VAPAM solution. Symptoms ranged from erythema, infiltration and itching of the skin, to severe irritation with burning redness, acute swelling and blistering of the skin. Two of the cases displayed punctiform cutaneous haemorrhages of a purpuric nature. Skin sensitisation tests in the same patients, showed acute positive cutaneous and epicutaneous reactions. These results indicate that humans occupationally exposed to a 10% VAPAM solution suffered from moderate or severe skin irritation. They also appeared to display strong skin sensitisation reactions to the formulation at subsequent exposure, but the non-irritating concentration of VAPAM was not determined for use in the challenge test. Case reports on dazomet, from the open literature, were used to establish an acceptable patch test concentrations for human experimentation. A particular case report mentioned contact dermatitis resulting from exposure to dazomet, but no further details were supplied.

4. DISCUSSION

Metham-sodium, dazomet and MITC can all be considered to be of moderate acute toxicity. Although not a likely route of exposure, the data suggest that MITC might be more acutely toxic by the oral route than metham-sodium (about 8-fold) or dazomet (about 4-fold), at least in rats. However, the oral LD_{50} values for both MITC and metham-sodium were quite variable. Thus, for MITC, there was a 3-fold range in values between studies and for metham-sodium, a 4-fold range. For dazomet, the LD_{50} values obtained from two studies, one using dazomet and the other the EUP, Basamid, were reasonably similar (between 400 and 650 mg/kg). This variability, together with the poor documentation of some of the metham-sodium studies, makes such comparisons between the chemicals difficult. A comparison of oral LD_{50} values in mice for metham-sodium and MITC suggests a similar, or at least only slightly greater, toxicity of MITC than metham.

In line with the acute oral toxicity of dazomet, MITC and metham-sodium, the acute sc toxicity in the rat and mouse, the acute ip toxicity in the rat and the acute inhalational toxicity in the rat, were greater for MITC than for dazomet, and similarly, acute inhalational toxicity in

the rat was greater for MITC than for metham-sodium. The magnitude of the differences was comparable for all three routes. In terms of systemic exposure to chemical, it is not clear why these differences exist if dazomet (and presumably also metham) is extensively metabolised to MITC in the body. It is possible that dazomet and metham are more poorly absorbed than MITC. There were limited details given on the products of dazomet metabolism, and it is possible also, that metham and dazomet are metabolised to other products as well as MITC.

In the rat, the dermal LD_{50} values for MITC and dazomet were higher than those for metham-sodium (in the order of 4-fold) (ie metham more dermally toxic than dazomet and MITC). These data are not consistent with the acute oral toxicity data (greater oral toxicity of MITC than of metham (or dazomet)). This probably reflects variability between studies because the acute dermal toxicity data for metham and MITC in the rabbit were consistent with the oral toxicity data.

Signs of acute toxicity were similar for all three compounds, in particular convulsions, shaking and tremors, salivation, lacrimation, initial lethargy. Changes observed upon necropsy were also similar for all three compounds, in particular haemorrhagic lesions most notably in the GIT, but also lungs and liver.

Chronic exposure to these chemicals is unlikely, except possibly in an occupational setting in which the most likely route of exposure might be inhalation (of MITC). No data were submitted on extent of absorption of MITC by the inhalational route. Similarly, no data were submitted on the extent of percutaneous absorption of any of these chemicals. Target organs of toxicity (systemic) of these chemicals are the liver, red blood cells and to some extent, the kidney. Chronic administration of MITC to rats and mice and of dazomet to rats (albeit by the oral route) was not associated with carcinogenicity. There was some evidence that metham might be teratogenic, but only at very high doses, whereas there was no such evidence for MITC and dazomet (tested at lower doses than metham because of embryotoxicity). It is unclear why metham appears to be less embryolethal than MITC and dazomet.

Whilst it is known that metham breaks down in soil to MITC, there is no information on its conversion to MITC by metabolism in animal tissues, and although this would appear to be likely, it is not known to what extent metham might be converted to MITC by metabolism in animals and what other metabolites might be formed. It is noteworthy that the related chemical, dazomet, which also breaks down in the soil to MITC, would appear to be largely absorbed (at least in rats) as MITC following oral administration (although this was not demonstrated unequivocally).

The major hazard of metham, MITC, and to a lesser extent, dazomet, in an occupational setting, would appear to be their local irritancy (skin, eye and lung) and sensitising effects. Thus, both MITC (technical) and metham-sodium (EUP) are severe skin irritants and MITC (technical) and metham (EUP) are severe and moderate eye irritants, respectively. Data on skin and eye irritancy are only available for technical MITC and the severity of irritancy due to the gaseous form is less clear. However, as expected, eye irritation was observed in an acute inhalation toxicity study in which rats were exposed to the vapour produced from liquid MITC (VORLEX 77). In contrast to MITC and metham-sodium, dazomet caused only slight dermal and ocular irritancy at comparable concentrations/doses. It is clear that dazomet is an inherently less irritant compound than MITC and metham-sodium. This lower ocular and dermal irritancy of dazomet than the other two compounds is not inconsistent with conversion of dazomet to MITC by animal tissues (extensive conversion presumably does not occur on the surface of the skin or eye). Nevertheless, dazomet might exert eye and skin (and lung) irritancy following conversion to MITC and volatilisation of the latter.

An acute inhalational toxicity study in rats also revealed the local irritancy of gaseous MITC, as moderate to severe lung congestion and areas of lung haemorrhage were observed in animals that died. Following use of these chemicals, inhalational exposure would mainly be to MITC, because metham-sodium is non volatile and dazomet has low volatility compared to MITC, and both are broken down in the soil to the volatile MITC. Volatile MITC could also be a source of systemic exposure by the dermal route, although no data were presented on the extent of either dermal or inhalational absorption of MITC. Public exposure, as well as occupational exposure, to MITC may occur following the use of these chemicals because of the volatility of MITC. The risk associated with such exposure is difficult to quantify because of lack of relevant data, in particular ambient concentrations of MITC following the use of metham-sodium (which may vary considerably depending on the weather conditions at the time of use).

Skin sensitisation due to metham-sodium is also an occupational risk. Both MITC and metham-sodium are skin sensitisers. Dazomet was not found to be a skin sensitiser under the conditions of the two studies conducted, but there have been literature reports of contact dermatitis in humans following exposure to dazomet, as well as to metham-sodium.

RECOMMENDATIONS

1. The main risk associated with the use of metham-sodium, MITC and dazomet appears to be due to their (and/or their breakdown product's) eye, skin and lung irritancy and skin sensitisation potential. These chemicals are appropriately scheduled in the SUSDP under S6 and therefore no change needs to be made to their current scheduling.

2. It is noted that, MITC, dazomet and metham-sodium have similar toxicological profiles, and appear to act through a common toxic entity. No change is recommended for the First Aid Instructions for the three compounds. The recommended safety directions are detailed below:

a) Metham sodium : The current SDs for Metham are:

Metham-sodium	AC EC LD all strengths	120 130 131 132 133 161 162 163 164 180 210 211 220 222 279 280 285 290 292 294 299 300 303 330 332 340 342 350 360 361 364 365 366

The avilable products are a soil fumigants (423 g/L), liquid soil fumigants (423 g/L), and foaming root fumigants (228 g/L). 423 g/L metham corrsponds to 510 g/L metham-sodium. On the basis that the active is the only ingredient which would contribute significantly to the toxicological profile of these products, and assuming a concentration of 510 g/L metham-sodium or less, the following SDs might be appropriate, based on hazard. It will be noted that there are no SDs related to PPE listed, as these will be supplied by Worksafe.

Amendments

Metham-sodium AC EC LD all strengths - amend entry to read:

Metham-sodium	AE EC LD 510 g/L/kg or less	129 131 133 207 162 163 164 180 220 222 223 309 330 331 332 342 340 341 342 343 340 341 343 **... ... ... (**PPE from Worksafe)

Prescription of SDs for metham-sodium in fumigant form needs to be considered further (hence 309). It is noted that a conservative approach to eye irritancy has been taken and thus SDs for a severe eye irritation on the basis that although the eye irritation is said to be moderate for a 37% solution, the skin irritancy is severe in the same concentration. It seems somewhat unusual for a product to be less damaging to the eyes than to the skin.

b) MITC: The existing SDs for MITC are:

Methyl isothiocyanate	All strengths	130 131 132 133 206 162 161 163 164 210 211 220 222 230 279 280 283 290 292 294 298 301 330 331 332 342 340 341 342 343 340 341 343 370

Information on formulations and use pattern/application methods for each product are usually used in developing SDs. However, given that MITC is not used in Australia, Safety Directions are to be based on the 96% TGAC.

Given the toxicological profile of technical MITC, the following SDs, based on hazard, would appear to be appropriate.

Amendments

Methy isothiocyanate - amend entry to read:

Methyl isothiocyanate	All strengths	100 130 131 132 133 205 206 162 220 222 223 230 207 164 309 340 341 343 330 332 340 342 **... ...** PPE from Worksafe) **... ... ...**

(note: 309 applies to detailed instructions for safe use which appear in State regulations).

c) Dazomet: Dazomet EUP is Basamid Granular which is a 97% formulation of dazomet, comprising granules. The only excipient listed is 0.1% silica gel. Use pattern is as a soil fumigant which is applied directly to the soil in granular form.

Current SDs are:

Dazomet	GR 980 g/kg or less	120 130 133 161 162 163 164 210 211 220 221 279 283 290 294 297 320 340 342 350 360 361 363 366

Given the acute toxicological profile of dazomet, there is no evidence to suggest that a change to the existing safety directions, based on hazard, is required. Worksafe Australia may wish to review the safety directions relating to PPE.

3. Whilst not within the current scope of this review, the issue of whether MRLs are relevant and/or required for these compounds may need to be considered by the National Registration Authority. In the past, it has been considered questionable whether exposure of the public to these chemicals via food residues is an issue. This has been due to the instability of metham-sodium and dazomet (their break down to MITC in the soil), and because of the volatility and toxicity to plants of MITC. The setting of ADIs and MRLs for these chemicals would, however, appear to be inconsistent. To date, no ADIs have been set for metham or MITC, whereas an ADI has been set for dazomet, indeed this ADI is proposed for amendment following the review of more recent data. In addition, there are no MRLs for MITC or dazomet, but MRLs (at or near the limit of detection) have been set for metham. The residue issue does not, in any way, impact on the decisions on scheduling or occupational safety directions for these compounds.

4. WSA should consider by-stander exposure to gaseous MITC.

SUMMARY OF TOXICOLOGICAL HAZARD (TGAC*)

	MITC	METHAM	DAZOMET
Worst Oral LD_{50} in Rat: (mg/kg)	72	450	415
(Range of oral LD_{50})	(72-220)	(450-1800)	(415-about 640)
Worst Oral LD_{50} in Other Species (mg/kg)	90 (mice)	50 (mice)	not available
Worst Dermal LD_{50} (mg/kg)	263 (rabbits)	650 (rats)	>2000 (rats)
Worst Inhalation LC_{50} in Rats (mg/m^3)	540	>4700	8400
Skin Irritation:	severe (rabbit; TGAC)	slight - severe (rat & rabbit; 3 - 37% aq)	slight (rabbit; EUP)
Eye Irritation in Rabbit	corrosive (TGAC)	mild-moderate (3 - 50% aq)	slight (TGAC /EUP)
Skin Sensitisation in Guinea pig	weak	moderate-strong	nil
T value:	7	20	40

Remarks: Contact dermatitis observed in humans exposed to VAPAM (10% metham-sodium formulation) and in humans exposed to dazomet

* TGAC unless otherwise specified. Note that in the case of dazomet, it would be expected that there would be little difference between the toxicity of the TGAC and EUP, given that the difference between the two forms is only one of particle size (larger for Basamid Granular than for the TGAC).

Occupational Health & Safety Assessment Report of Metham-Sodium (Soil Fumigant Use), Dazomet and Methylsiothiocyanate

1. INTRODUCTION

Metham-sodium (referred to in this report as metham), is a dithiocarbamate compound, with fungicide, nematocide, herbicide and insecticide activity. Metham is registered in Australia in several end use products (EUPs), for the control of weeds, nematodes, symphylids (not in Tasmania), fungi, soil insects and other soil-borne pests in ornamentals, food and fibre crops and tobacco.

Dazomet (one product) is registered for the control of nematodes, soil inhabiting insects, germinating seeds of weeds and fungi. Methyl isothiocyanate (MITC), a soil fumigant no longer registered in Australia, is the major degradation product of metham and dazomet.

This occupational health and safety (OHS) report assesses the currently registered end use situations for metham and dazomet and makes recommendations on their future use.

MITC is also considered, being the active component of both metham and dazomet.

Information was obtained from registrants of metham and dazomet, the Therapeutic Goods Administration (TGA) Toxicology Reports (TGA, 1995, 1996), Committee papers, scientific literature, a number of State and Territory Agriculture Departments and other organisations. Original submissions for registration were not available from the National Registration Authority for Agricultural and Veterinary Chemicals (NRA).

State and Territory Agriculture advice was also formally sought via RLC members. Responses were received from Department of Agriculture, Victoria.

1.1 Identity of chemicals

Refer to Table 1 for details.

1.2 Reported adverse incidents in Australia

- In August 1991, the Drugs and Poisons Schedule Standing Committee (DPSSC) considered some poisoning incidents from Victoria. A few incidents were reported where persons were affected by fumes when metham was applied through a fixed sprinkler irrigation system in neighbouring properties. Irritation of the nose, eye and throat were reported. It was noted that many farmers use high pressure impact sprinklers through fixed irrigation systems. In such systems, accuracy is not generally possible and high pressure is required for effective coverage.

Web users: the following landscape pages may not print satisfactorily. See http://www.affa.gov.au/nra/chemrev and select the attachment to the Metham Sodium report for landscape copies.

Table 1 Identity of chemicals

Chemical	CAS No	Physical properties	Vapour pressure	Solubility
Metham (a)	144-54-7 (metham) 137-42-8 (metham-sodium anhydrous) 6734-80-1 (metham-sodium dihydrate)	greenish-yellow liquid with a sulphide odour	not available (not considered to be volatile)	appreciably soluble in wat
Dazomet (a)	533-74-4	white to off-white solid, with a weak intrinsic odour	1.4 kPa @ 20°C (low volatility)	solubility in water is low (g/100 g @ 20
MITC (a)	556-61-6	brown oily or clear yellow liquid, with a pungent horseradish-like smell	2.76 kPa @ 20°C (moderate volatility)	poorly soluble water (8.2 g/L

(a) In Schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) (Australian Health Ministers' A
(b) Both processes yield mainly MITC. Other major products of hydrolysis are carbon disulfide and methylamine. Minor hy sulfur and 1,3-dimethylthiourea. Major products of photolysis are N-methylthioformamide, methylamine and elemental s include N-methylformamide, carbon disulfide, carbon oxide sulfide and hydrogen sulfide (TGA, 1996).

- The Committee also considered another complaint from Bellarine Rural City Council. A flower grower frequently applied undiluted metham by tractor mounted boom spray, at a rate of approximately 480 L/ha. The boom was 1 metre above the soil surface. Spraying was conducted in relatively still conditions and overspray did not appear to be a problem. Several complaints were received from adjacent residents. Eye irritation occurred several hours after spraying had been completed. The health surveyor for the Council also experienced these effects. Fuming was noticed at a distance of up to 20 metres from the application site, 3 hours after spraying was completed.

  The committee concluded that spraying, irrigation and flood irrigation were not appropriate methods of metham application. The Advisory Committee on Agricultural Chemicals (ACAC) agreed to this in principle.

- In May 1994, a worker in Victoria reported adverse effects when fumigating a small nursery site. This complaint initiated the NRA Special Review. According to the report, the worker had 25 years experience as an orchardist and had completed a Farm Chemical Users Course. He applied metham using a hand held boom (from a motorised spray unit) then incorporated it into the soil with a tractor mounted rotary hoe and sealed with black plastic. He wore protective clothing recommended on the product label, including respirator and goggles. Weather conditions were such that there was minimal spray drift. During application and soil incorporation, the vapours caused severe eye irritation and nausea. During the process of incorporation, the gases were visible and vapours were noted by a person some distance away.

- The Health Department of Western Australia has records of adverse health effects following the use of metham. In one case, metham was applied through a sprinkler system by a local market gardener. Severe eye irritation and nausea were experienced by customers and neighbours. In a separate incident, householders in a market garden area complained of eye and skin irritation and nausea when metham was applied through a reticulation (but not sprinkler) system.

1.3 Overseas regulatory status

United States

In 1991, the US Environment Protection Agency (US EPA) instructed registrants of metham, through a data call-in notice, to complete a range of acute, subchronic and chronic mammalian tests, exposure data, chemical data and ecotoxicity data. The US EPA is awaiting/reviewing data on metham, dazomet and MITC (US EPA, 1994).

US metham labels require the following protective equipment to be worn by workers carrying out any operations that are likely to involve direct contact with the product, including mixing/loading, equipment calibration or adjustment, clean up and repair of application equipment, sampling, clean up of spills, fumigant transfer and rinsate disposal. This equipment is also required for any operations occurring within 6 feet of unshielded, pressurised hoses containing metham products.

- A properly fitted half-facepiece respirator with organic vapour cartridge;
- Non-venting chemical goggles (or a full- facepiece respirator with organic vapour cartridge);
- A body covering with long sleeves and long pants;
- When a closed system is not used, mixer/loaders should wear chemical resistant aprons or cloth overalls; and
- Chemical resistant gloves and boots.

Workers operating or monitoring application equipment or entering treated areas within 48 hours of application should wear chemical resistant footwear and a body covering with long sleeves and long pants. In addition, the following protective equipment should be available to workers operating tractor drawn application equipment, monitoring application equipment or re-entering treated areas within 48 hours after application:

- A properly fitted half-facepiece respirator with organic vapour cartridge and non-venting chemical goggles (or a full- facepiece respirator with organic vapour cartridge) to be worn when odour is detected; and

- Chemical resistant gloves (to be worn if direct contact with the product is likely).

In July 1991, the California EPA issued a warning to pregnant women to avoid exposure to metham. Both metham and MITC were placed on California's list of most highly controlled chemicals. Use of these chemicals is only permitted when persons are adequately trained and hold a permit for their use (The Bureau of National Affairs Inc., 1994).

2. TOXICITY

2.1 Summary of experimental toxicology

Refer to TGA (1995, 1996) for details.

Table 2 summarises the relevant toxicology endpoints for short- and long-term occupational exposure.

The minimum lethal human dose and the maximum tolerated human dose for MITC is unknown (Saratext System).

2.2 Human/animal metabolism It is believed that metham and dazomet are metabolised to MITC. However, the extent of metabolism of metham or dazomet to MITC following exposure to human or animal skin or lung epithelium is unknown.

2.3 Most sensitive species The most sensitive sign of exposure to MITC reported in the literature is ocular mucosal irritation in cats, at airborne concentrations of 70 ppb or 0.2 mg/m^3 (Nesterova, 1969 cited in Alexeeff et al., 1994).

2.4 Hazard classification Metham, dazomet and MITC are classified as hazardous substances, under the National Occupational Health and Safety Commission (NOHSC) Criteria. They are listed on the List of Designated Hazardous Substances (NOHSC 1994a).

Table 2: Toxicological end points obtained from animal studies relevant to short-term and long-terr

Chemical	Worst acute oral toxicity (LD_{50}) (mg/kg)	Worst acute dermal toxicity (LD_{50}) (mg/kg)	Worst acute inhalation toxicity (LC_{50}) (mg/m^3)	Eye irritation	Skin irritation
Metham (a)	450 (moderate: rat)	650 (moderate: rat)	>4700 (low: rat)	Moderate: rabbit (only 3% and 37% aqueous solutions tested)	TGAC[1] -Corrosive (rabbit) 37% aqueous - severe irritant (rats and rabbits) 3% aqueous - slight irritant (rats and rabbits)
Dazomet (b)	400 (moderate: rat, females)	>2000 (low: rat)	8400 (very low: rat)	Slight: rabbit (TGAC and EUP)	50% aqueous -slight irritant (rabbits) TGAC - not tested
MITC (c)	72 (moderate: rat)	263 (moderate: rabbit)	540 (4 hour: moderate: rat)	TGAC - Corrosive: rabbit	TGAC - Severe: rabbit

(a) All registered metham-based EUPs are 50% in water. Hence, the acute toxicity profile of the products is expected to be si
1 - Technical grade active constituent
(b) It is envisaged that the TGAC and EUP for dazomet will have similar toxicity because the difference between the two forr
(c) No EUPs registered in Australia
(d) The NOELs used in the Risk Assessment
(e) Calculated assuming a minute volume of 29 L and a daily exposure of 4 hours (the duration of exposure in the rat inhalati

2.5 Human health effects observed after environmental or occupational exposure incidents

This section contains information derived from epidemiological studies and case studies of persons adversely affected after skin contamination or exposure to fumes. The degree of exposure to metham, dazomet, MITC or other degradation products with toxic or irritant properties (eg. hydrogen sulfide, methylamine and carbon disulfide (CS_2)), is largely undefined in these studies, although it is known to have occurred. A comparison of odour and irritant thresholds for metham and its degradation products is given in Table 3. This section does not contain information derived from measured field worker inhalation exposure studies, dealt with separately in Sections 3.4.

Metham and MITC

Metham and MITC are considered together. The health effects of both are interrelated because metham undergoes hydrolytic decomposition to MITC when in contact with moist skin and in the environment. Severe cases of contact dermatitis and/or skin sensitisation were reported in workers using metham as a soil disinfectant (Wolff and Jung, 1970; Richter, 1980) or involved in the clean up of the 23,500 kg metham spill in the Sacramento River, California in 1991 (Koo et al., 1995).

Effects may result from direct contamination on the skin or by the wearing of wet contaminated clothing, or result from the environmental (ie. airborne) contamination with vapour. Individuals relying on wearing protective equipment only when odour is detected may not be protected against adverse effects. Nesterova (1969) cited by Kreutzer et al. (1994), suggested that MITC was capable of causing symptoms at concentrations below its odour threshold. This is supported by the more recent examination of health effects following the metham spill in the Sacramento River (Cone et al., 1994; Kreutzer et al., 1994).

Wolff and Jung (1970) reported on contact dermatitis experienced by rural workers applying a 10% metham solution via an injection lance, directly into the root area of potato crops, in Germany. The patients exhibited symptoms ranging from erythema, infiltration and itching, to severe inflammation with burning, swelling, blistering and cutaneous haemorrhages. There was a latent period before symptoms developed. These workers had experienced substantial direct skin contact with metham liquid, as well as exposure through contaminated clothing. Patients demonstrated a positive response to patch testing and when exposed to metham vapour. Additional worker controls were instituted after this investigation, among them that only freshly diluted solutions should be used and that workers previously affected by metham should not continue to work with the chemical.

Richter (1980), a dermatologist, reported on a number of occupational exposures to metham and concluded that MITC was a strong contact sensitiser.

Koo et al. (1995) reported that a high proportion of a certain worker group involved in cleaning up the Sacramento River over a two day period, experienced dermatitis particularly of the feet, legs and ankles, about one week later. This group had continued working in wet clothing. Other workers who were able to change into dry clothing immediately following contamination did not report experiencing dermatitis. The river water concentration of MITC was 20-40 ppb at the time of exposure. The authors noted that this was below the concentration normally associated with clinical findings (≥ 1%), but speculated that the clean up workers may have been more susceptible because of the length of time they were in contact with the water, combined with the continued rubbing of skin against contaminated clothing and footwear.

Schubert (1978) investigated using patch testing, the component in metham likely to be allergenic. He suggested that MITC rather than metham was more likely to be the allergen because the isothiocyanate group easily binds to protein. There may be a latent period before skin effects are manifest.

The Sacramento River spill prompted a number of studies on the health effects in residents and those working in the area, following environmental exposure to airborne residues. The scale of this event is not directly comparable to the short-term exposures likely to be experienced by end users of metham and dazomet products, however the reports include useful human toxicity data relevant to bystanders and workers. Topical effects experienced by workers exposed to the metham spill in water have been described above. Kreutzer et al. (1994) conducted an epidemiological study on those seeking medical attention in the month following the spill. The most common symptoms reported were headache (63.8%, more frequently reported in those detecting an odour, more likely to be hydrogen sulfide (H_2S) than MITC), eye and throat irritation and nausea, days and weeks after the spill. Not all persons who experienced symptoms detected odours. The frequency of weakness, nervousness and flushing was significantly higher among those not detecting an odour. Some late symptom reports were received. The reasons for this are unclear, although the authors proposed a number of possible explanations not necessarily related to airborne exposure. Airborne exposure monitoring for this locality indicated that exposures higher than the irritant threshold would only have been experienced within the first 1-2 days. A few cases were hospitalised, but there were no fatalities. No adverse pregnancy outcomes were recorded. The authors discussed the influence of the timing of the spill, air and water flows and the season on the airborne concentrations of MITC.

Cone et al. (1994) reported on persistent respiratory health effects in the resident, including worker, population above. Twenty new cases of persistent irritant-induced asthma were identified, of which 17 met the criteria for reactive airways dysfunction syndrome (RADS) (persistent asthma after high level exposure to irritant vapours). Not all subjects detected an odour. Exposure time had been as short as four hours. There were a number of cases where pre-existing asthma was exacerbated. Symptoms were still present several months after exposure. Modelled airborne MITC during the first three days, ranged from 140-1600 ppb (monitoring data not available).

These levels are possibly irritating to humans. The authors were unable to make any conclusions as there was an inconsistent exposure-symptom relationship using distance as a surrogate for exposure.

Table 3: Comparison of odour thresholds and irritant thresholds for metham, dazomet, MITC and degradation products

	Odour threshold	Irritant concentrations or thresholds
Metham	Not available	500 ppm or 0.05% in water; non-irritant, used in patch testing (1)
Dazomet	Not available	Not available
MITC	100 ppb (2)	70 ppb mucosal irritation in cats (2)
	100 - 500 ppb (3)	<200 ppb airborne; caused symptoms (4)
		20-40 ppb in water; irritant dermatitis(5)
		Increasing to 10,000 ppb eye and respiratory tract irritation seen in a number of species (6)
		10 ppm, inhalation NOEL in a 3 month rat study for systemic effects at 45 ppm (7)
		LC50 - 540 mg/m^3; rat, 4 hours (7)
H_2S	1-2 ppb (8)	10,000 ppb (8)

(1) Richter (1980)
(2) Nesterova (1969), cited by Kreutzer et al (1994)
(3) Nesterova (1969) cited by Cone et al (1994)
(4) Kreutzer et al (1994), based on model data and odour perception
(5) concentrations of MITC in the Sacramento River, measured 7 days after the metham spill. Workers were allowed to enter the water at this stage but developed irritant dermatitis (Koo et al., 1995)
(6) Cone et al (1994)
(7) TGA (1996)
(8) Ellenhorn and Barceloux (1988) cited by Kreutzer et al (1994)

Other degradation products may also be involved. For instance, H_2S is an eye and respiratory irritant at low concentrations (10,000 ppb) but causes systemic effects such as nausea, vomiting, headache, cardiac arrhythmias, dizziness and confusion at higher concentrations. In contrast to MITC, the odour threshold of H_2S is lower (1-2 ppb) than the irritant threshold. Hence, mechanisms to control exposure to H_2S vapour can be more effective than for MITC.

Dazomet and MITC

Richter (1980) reported severe dermatitis in a worker who spilt dazomet inside her rubber boots when treating soil. The worker was patch test positive to a 0.05% aqueous solution of metham (Vapam). She also demonstrated an inflammatory response in the liver, which despite some complications, was ascribed by the author to the percutaneous absorption of MITC.

Another case of allergic contact dermatitis caused by dazomet was reported by Warin (1992). Dazomet was used as a biocide in a paper mill. The author referred to two other earlier cases, following occupational exposure.

2.6 Reference exposure limits

There is no ACGIH, OSHA or NOHSC exposure standard for MITC, but there is a Russian exposure standard of 0.1 mg/m^3 (STEL), referred to in industry submitted data in Part 2 of the OHS review.

Alexeeff et al. (1994) determined Reference Exposure Levels (RELs) for certain adverse health effects in a diverse human population exposed to MITC for one hour. They covered death or life-threatening effects, disability and discomfort and were determined using a no-observable-adverse-effect-level (NOAEL), lowest-observable-adverse-effect-levels (LOAEL) and an uncertainty factor (UF). UFs of 100 and 1000 were considered appropriate when using NOAELs and LOAELs respectively. The RELs determined were as follows:

To prevent discomfort - 0.0014 mg/m^3 or 0.5 ppb (based on ocular irritation in cats)

To prevent disability - 0.13 mg/m^3 or 40 ppb (based on severe upper respiratory tract irritation)

To prevent life threatening effects - 0.488 mg/m^3 or 150 ppb (based on non-lethal levels in mice).

3. OCCUPATIONAL EXPOSURE

3.1 Registered products

Metham

Several metham products are currently registered in Australia as soil fumigants. These EUPs are formulated as suspension concentrates and contain 423 g/L metham as the sodium salt (corresponding to 510 g/L metham-sodium) and water. All EUPs are hazardous substances because they contain ≥ 5% metham.

Metham-based agricultural products are packed in containers ranging from 1 L to 1200 L.

Dazomet

BASAMID GRANULAR, a microgranular formulation containing 970 g/kg dazomet, is the only dazomet EUP currently registered as a soil fumigant in Australia. This EUP is a hazardous substance, as the concentration cut-off is 25%.

The difference between the TGAC and EUP is that particle sizes are larger for the EUP. In the production process, silica gel is added to the TGAC to prevent electrostatic charging of the EUP. The particle size distribution of the EUP is as follows: 0.4%-0.8% particles <100 μ, 56%-64% particles <200 μ and 100% particles <400 μ.

The product is dust free (BASF Aktiengesellschahft, 1989) and packed in 20 kg drums.

3.2 Estimated numbers of end users

It is not possible to give an accurate estimate of the number of end users of metham and dazomet. Estimates from registrants indicate there may be approximately 2000 farmers using metham and 150 using dazomet Australia-wide.

3.3 Use patterns

This information was obtained from product labels, except where otherwise stated.

Metham

In Australia, metham is usually applied yearly, however, in soils cropped more frequently it may be used 2-3 times/year (WA Department of Agriculture).

The efficacy of metham soil fumigation is dependent upon soil preparation (cultivation and moisture content), humidity, ambient and soil temperature at application and site treatment immediately after application (rolling and sealing in fumes using water or plastic sheeting). The plant back period (interval between application and planting) is variable. It depends upon soil type, temperature, moisture, organic matter content of the soil and the amount of spray applied. Treated areas may require light cultivation 5-7 days after treatment to promote drying.

A "germination test" (sowing of an indicator crop, usually lettuce or radish) should be carried out approximately 7 days before the main crop, to determine whether toxic fumes still remain in the soil. The plant back period varies from 14-60 days after treatment.

Specific details regarding all the above appear on metham product labels.

Application rates and methods

For most uses, the products are diluted with water prior to application. Once the products are mixed with water, the mixture should not be allowed to stand because metham is unstable and undergoes hydrolysis when diluted.

The product dilution rates are similar for all metham products. The application methods for various treatment sites are summarised in Table 4.

The table indicates that for field applications, large volumes of metham product are needed (up to 500 L per hectare in non-irrigation water applications) and high concentrations of working strength solutions (up to 51% metham) need to be handled by workers.

For more limited areas, eg. lawns and seed beds and controlled treatments, eg. potting soil, smaller product volumes and lower metham concentrations are required.

Table 4: Use pattern for metham

Use situation	Soil Injection	Rotary Tiller	Irrigation
Seed beds, lawns and limited areas	25-50 L product in 50 L water per 1000 m^2 (50% - 100% product and **25%-51% metham-sodium**) Injection is followed by rolling and light watering or soil injection directly ahead of bed shaper.	1.1 L product in 12 L water per m^2 (9% product and **5% metham-sodium**) The solution is sprayed or sprinkled in front of the tiller, cultivated in, soil rolled over and watered.	-
Field application (total area)	250-500 L product in 400-700 L water/ha (36% - 100% product and **18%-51% metham-sodium**)	250-500 L product in 400-700 L water/ha (36% - 100% product and **18%-51% metham-sodium**)	(a) Approved irrigation system trickle irrigation, linear or cent systems[1] - 600-800 L product p 1100 L water (55%-89% produ **27%-45% metham-sodium**) (b) Flood irrigation - 610-790 l product/ha in a minimum of 15 water.
Field application (beds and rows)	250-500 L product in 400-700 L water/ha (36% - 100% product and **18%-51% metham-sodium**)	250-500 L product in 400-700 L water/ha (36% - 100% product and **18%-51% metham-sodium**)	Trickle irrigation - 250-800 L/h (100% product and **51% meth sodium**). To be applied to bed previously prepared with trickl and plastic mulch.

[1] Some labels specifically indicate that these product may not be used through fixed, portable or solid set systems, travellir system using impact sprinklers, operating at high pressures or those causing drift.

Table 4, Cont: Use pattern for metham

Use situation	Soil Injection	Rotary Tiller	Irrigation
Potting soil		1.1 L product per 10-12 L water per 10 m^2 (9%-11% product and **5%-6% metham-sodium**)	
Tobacco plant beds			Approved irrigation system - 9.75 L product in 700-900 L water per 100 m^2 (1%-1.3% product and **0.5%-0.7% metham-sodium**).

Source: Metham product labels

Dazomet

Dazomet is available in a granular formulation for seedbed, broadacre and bulk soil treatment. The efficacy of dazomet fumigation is dependent on site preparation (cultivation and soil temperature and moisture content). Granules should be immediately incorporated into the soil and the surface sealed by water, plastic sheeting or rolling. Bulk soil may be stored in sealed bins. Soil should be aerated within 1-2 weeks of treatment. A germination test should be conducted before planting crops. Tests may commence within 2-6 weeks after treatment.

Application methods

Specific instructions appear on the label for BASAMID GRANULAR.

Granules may be spread manually, using small mechanical (drop) spreaders or gloved hand, or mechanically, via large mechanical spreaders mounted on tractors. The granules should be incorporated by rotary hoe or hand hoe, prior to sealing.

The registrant informed Worksafe Australia the maximum area likely to be treated per day is 1 ha using tractor mounted spreaders and 0.05 ha during hand spreading.

Application rates

For seedbeds and broadacre sites, the product application rate is 340 kg/ha - 680 kg/ha (equivalent to 35 g/m^2 - 70 g/m^2), depending on the pest. For bulk soil, the recommended rate is 150-220g/m^3, irrespective of pest.

3.4 Occupational exposure studies - metham

The four worker studies assessed deal only with MITC emissions in air following metham treatment. Degradation data indicates that soil conditions influence the conversion rate of metham to MITC. The worker studies indicate that application conditions also influence MITC emissions and worker exposure.

Studies (1) and (2) were sponsored by the Metham-Sodium Task Force. They compare MITC residues during different application methods. Sites are chosen in Washington and Arizona, to cover different climate zones.

(1) Pan-Ag Study No EF-91-360, August 1993

Rosenheck L (1993a) Worker Mixer/Loader and Applicator Exposure from Field Applications of Metham-Sodium, Pan-Ag Study No EF-91-360, August 1993, Sponsor Metham-Sodium Task Force c/o ICI Americas, Inc. (UCB Chemicals response to data call-in by the NRA).

The study was conducted under US EPA Pesticide Assessment Guidelines, Subdivision U 133-3 (Dermal Passive Dosimetry Exposure) and 133-4 (Inhalation Passive Dosimetry Exposure). It assessed potential inhalation exposure of CS_2 and MITC during loading and applying metham in fields by soil injection or fixed sprinkler chemigation.

The study was conducted in pre-cultivated fields in Yuma County, Arizona, USA. A water miscible 33.4% formulation of metham was used at the maximum US application rate of 100 gallons per acre (1135 L/ha or 356 kg ai/ha). The maximum application rate on Australian labels for chemigation methods is 800 L/ha (480 kg ai/ha) and 700 L/ha (360 kg ai/ha) for whole field application by soil injection or incorporation. All metham products currently registered for agricultural use in Australia are suspension concentrates containing 51% metham-sodium.

Environmental conditions such as temperature, relative humidity, wind speed and direction and soil temperature (at a depth of 3 inches) were recorded.

Potential inhalation exposure to CS_2 and MITC were measured using two personal air sampling pumps, each attached to a charcoal vapour-collection tube, worn on the worker's shirt lapel.

Loaders and applicators wore long-sleeved shirts, and long pants. In addition, loaders wore rubber boots, goggles, respirators and nitrile gloves. Applicators were provided with goggles, respirators and nitrile gloves to wear at their own discretion or when odour was detected.

For both trials, metham was stored in a 6000 gallon bulk storage tanker. Field fortification samples were prepared for MITC and CS_2, using duplicate sets of charcoal vapour-collection tubes attached to pumps. These samples were left out for the duration of one application replicate. Control samples were used to determine background MITC and CS_2 levels. Control sampling was conducted during the entire monitoring period of each trial, at an area distant from the application.

All samples were stored and transported for analysis by Morse Laboratories, California, where the analytical phase of the study was conducted. MITC and CS_2 levels in the filters were analysed using gas chromatography. Method validations were performed to demonstrate the validity of the methodology used. The Minimum Quantitative Level (MQL) value for MITC and CS_2 is 1 μg. This value is used when residue levels were less than MQL.

Inhalation residues were adjusted according to field fortification recoveries. Calculations were based on a breathing rate of 29 L per minute for an average male doing light work (US EPA (1987) Subdivision U Guidelines).

The Morse Laboratories Inc. report is included in the submission but not commented upon further here. The Rosenheck report presents and comments on quality control data.

Shank injection trial - method and results

There were ten loader replicates and ten applicator replicates.

Each loader replicate was the length of time required to load sufficient metham for one hour's application, ie. a minimum of 100 gallons (379 L). This ranged from 4-17 minutes (average 7 minutes). Applicator replicates were approximately 1 hour, the range was 60-78 minutes, with an average of 66 minutes.

The shank injection rig consisted of a 200 gallon tank secured above three tool bars. There were seven shanks each consisting of 3 horizontal blades and two nozzles. Closed- and open-cab vehicles were used to pull the shank injection rig. Closed-cab vehicles used charcoal (2 replicates) or cellulose (4 replicates) filters.

Loaders were not required to dilute the metham and could directly transfer it from the bulk tanker to the spray tank. They transferred the metham using a hose and couplers. When the tank was full, the worker closed the valves and disconnected the hose from the spray tank end only.

The loaders using the enclosed transfer system handled an average of 232 kg metham over the measurement time of approximately 7 minutes. Two workers comprised the ten replicates; only one worker wore goggles and a respirator although these items were prescribed. Airborne CS_2 was below the MQL. Airborne MITC was an average of 0.775 mg/hr (<MQL - 2.01 mg/hr) and 0.000282 mg/kg ai handled (maximum of 0.000611 mg/kg ai handled). A certain amount of metham spillage was associated with the transfer in all cases. In two instances, it was more than usual but did not result in airborne residues greater than the average.

The applicators stayed in the cab during the whole application replicate except when performing maintenance work on tractor or injection equipment. The shanks were fully inserted into the ground before metham was applied at 40 psi. A rotary tiller immediately following the injection equipment further incorporated the metham. This was followed by a roller to seal the surface. At the end of a pass, the spray was shut off before the shanks were lifted out of the ground.

Two workers made up the ten applicator replicates. One of these used a closed cab, with a charcoal filter for Replicates 1 and 2 and a cellulose filter for Replicates 3-6. This worker reported that the charcoal filters were more effective than the cellulose filters in controlling exposure to fumes. This observation is supported by MITC residues, which are lower where charcoal filters are used. Replicates 8-10 relate to the open cab. Replicates covered an average of 226 kg metham over a monitoring period of 66 minutes. Details of airborne residues for applicators coupled with airborne exposure incidents are given in Table 5. Airborne CS_2 is below MQL for all but 3 replicates (Replicates 3,4,8). Replicates 4 and 8 had the highest CS_2 and MITC residues. Airborne MITC averaged 2.04 mg/hr (range 0.301 - 6.71 mg/hr) and 0.0109 mg/kg ai applied (range 0.00138 - 0.0458 mg/kg ai applied).

In three replicates, equipment failure (tractor or injection equipment) caused the applicator to leave the cab and effect repairs during the application time. The only worker reporting fumes used a closed cab and subsequently used a respirator. The applicators in open cabs all wore respirators and goggles and no exposure to fumes is reported.

Sprinkler system trial - method and results

There were ten replicates each for metham loading and application.

The sprinkler system consisted of metal sprinkler lines containing sprinkler heads. Three sprinkler lines were used per replicate. An injector pump was used to pump the metham solution from the nurse tank into the sprinkler line.

Loaders conducted two closed transfer operations. Firstly, they filled a holding tank located on a truck with metham from the storage tanker, using a hose and couplers. Secondly, after disconnecting the hose, the worker drove the truck to the field and filled up the nurse tank using another hose. During disconnection, metham was found to drip onto the hands and ground.

A loader replicate was the length of time required to load sufficient for 4 hours application, at a rate of 100 gallons/ha. The loaders were monitored for an average of 63 minutes (range 43-78 minutes) and transferred 509 kg metham (range 288-577 kg) over this time. All airborne CS_2 was below the MQL. Airborne MITC averaged 1.50 mg/hr (range 0.134 - 4.75 mg/hr), 0.00292 mg/kg ai handled (0.000289 - 0.00792 mg/kg ai) and 0.119 mg/kg bw/8 hours (up to 0.320 mg/kg bw/8 hours). A certain amount of metham was spilt each time the hose was removed from the nurse tank. Loaders assisted with application equipment maintenance during two replicates and direct spillage on a worker was noted in a third. More of these incidents resulted in airborne MITC residues above the average. All loaders wore protective equipment including respirator and goggles. No reports of fuming are mentioned.

Applicator replicates were approximately 4 hours each. During this time, an average of 502 mg metham (range 493-526 kg) went through the sprinkler system.

At the beginning of each replicate, the applicator walked into the field and manually turned on three new sprinkler lines and closed off the previous three. At this time there could still be metham fumes from the previous application and workers would routinely use protective equipment. For the first 30 minutes of each replicate, only water was allowed to run through the lines. Applicators then checked for blocked or broken sprinkler heads and started the injector pump. The pump was checked about every half-hour. When adequate product was applied the worker turned off the injection pump. Metham application took approximately two hours per replicate. Water was applied to the field for the remainder of the replicate (approximately 1.5 hours). During application, the applicator remained in his car located 10-50 feet away.

Fixed sprinkler application was associated with metham fuming during this period, to the extent that applicators used respirators and goggles and also sought to remove themselves to the more protected areas of the field. Initially this was particularly relevant when workers entered the treatment area to deal with sprinkler lines and heads, but later was associated with changes in wind direction and gustiness. Eye irritation, from watering to extensive tearing was experienced, despite the fact that workers wore goggles. Odours were so strong during one replicate that application ceased for some time. In all but one replicate, CS_2 was below the MQL. Average airborne MITC was 2.6 mg/hr (range 0.143 - 4.96 mg/hr) and 0.0208 mg/kg ai handled (0.00114 - 0.0404 mg/kg ai) and 0.249 mg/kg bw/8 hours (range 0.0144 - 0.483 mg/kg bw/8 hours). Higher airborne residues were observed for those workers experiencing the effects of MITC fumes. Details of airborne residues and potential exposure incidents are given in Table 6.

Results of the trials demonstrate higher airborne MITC residues with the fixed sprinkler method, ie.

- loaders (shank equipment) - 0.000282 mg/kg ai handled
- loaders (fixed sprinkler) - 0.00292 mg/kg ai handled

- applicators (shank equipment) - 0.0109 mg/kg ai handled
- applicators (fixed sprinkler) - 0.0208 mg/kg ai handled

The same is found for residues expressed as mg/hr, which are higher for fixed sprinkler method. Residues for loaders were less than for applicators.

Residues associated with fixed sprinkler loaders were higher than those for shank equipment loaders. Fixed sprinkler loaders performed two transfer operations.

Fixed sprinkler residues are approximately twice those of tractor drawn equipment operators. Sprinkler applicators reported fuming and tearing to a greater extent than shank injection applicators.

Table 5: Airborne MITC and potential exposure incidents when applying metham using shank inje

Replicate number (Rep), **worker ID**	**Cab type**	**Eye and respiratory protective equipment**	**Inhalation exposure to MITC (mg/kg ai handled)**	**Inhalation exposure to MITC (mg/hr)**	**Potentia**
Rep 1: Worker B	closed cab with charcoal air filter	None	0.00187	0.301	Equipmen
Rep 2: Worker B	closed cab with charcoal air filter	None	0.00240	0.494	
Rep 3: Worker B	closed cab with cellulose air filter	Respirator and goggles	0.00932 (a)	1.97	Tractor pr to the filte on during
Rep 4: Worker B	closed cab with cellulose air filter	Respirator and goggles	0.01220 (a)	3.12	
Rep 5: Worker B	closed cab with cellulose air filter	Respirator and goggles	0.0110	2.70	A lot of pr connected disconnec
Rep 6: Worker D	closed cab with cellulose air filter	Respirator and goggles	0.0110	2.70	
Rep 7: Worker D	Open cab tractor	Respirator and goggles	0.00346	0.774	
Rep 8: Worker D	Open cab tractor	Respirator and goggles	0.0458 (a)	6.71	Personal a and replac
Rep 9: Worker D	Open cab tractor	Respirator and goggles	0.0102	1.23	Worker tu completely
Rep 10: Worker D	Open cab tractor	Respirator and goggles	0.00138	0.385	
Average (b)			**0.0109**	**2.04**	

Source - Rosenheck L (1993a) Worker Mixer/Loader and Applicator Exposure from Field Applications of Metham-Sodiur Sponsor Metham-Sodium Task Force c/o ICI Americas, Inc.

(a) CS_2 levels were above the MQL (b) Arithmetic mean

Table 6: Airborne MITC and potential exposure incidents when applying metham using a sprinkler

Replicate number (Rep), worker ID	Eye and respiratory protective equipment	Inhalation exposure to MITC (mg/kg ai handled)	Inhalation exposure to MITC (mg/hr)	Potential exposure incidents
Rep 1: Worker C	None	0.00243	0.286	The injection pump leaked for the last 1.5 hours
Rep 2: Worker E	None	0.00114	0.143	
Rep 3: Worker E	Respirator and goggles	0.00411	0.505	
Rep 4: Worker E	Respirator and goggles	0.0241	2.95	Exposure to fumes caused by a change of wind d 20 min. Worker experienced tearing of eyes wh sprinkler heads, despite wearing goggles and res
Rep 5: Worker C	None	0.00938	1.17	Wind changed direction and blew metham fume
Rep 6: Worker C	Respirator and goggles	0.0242	3.02	Worker complained of strong fumes when he we direction caused watering of eyes
Rep 7: Worker C	Respirator and goggles	0.0404	4.96	Wind direction changed and strong fumes made
Rep 8: Worker E	Respirator and goggles	0.0386	4.82	Wind direction changed and strong fumes made
Rep 9: Worker E	Respirator and goggles	0.0268 (a)	3.32	Shifting winds caused the applicator to spend m zone
Rep 10: Worker E	Respirator and goggles	0.0365	4.79	Worker moved to the end of the field due to shif noticed, application halted and water applied for was resumed when odour dissipated. Worker re sprinkler.
Average (b)		**0.0208**	**2.60**	

Source - Rosenheck L (1993a) Worker Mixer/Loader and Applicator Exposure from Field Applications of Metham-Sodiur Sponsor Metham-Sodium Task Force c/o ICI Americas, Inc.

(a) CS_2 was >MQL (0.00016 mg/kg ai handled) (b) Arithmetic mean

(2) Pan-Ag Study No 92205, May 1993

Rosenheck L (1993b) Worker Loader and Applicator Exposure from Field Applications of Metham-Sodium, Pan-Ag Study No 92205, May 1993 Sponsor Metham-Sodium Task Force c/o ZENECA Ag Products (UCB Chemicals response to data call-in by the NRA).

The study was conducted under US EPA Pesticide Assessment Guidelines, Subdivision U 133-4 (Inhalation Passive Dosimetry Exposure). It assessed potential inhalation exposure to CS_2 and MITC during loading and applying metham in fields.

The study was conducted in Grant County, Washington, in November 1992. It investigated ambient airborne exposure during metham application by rotary tiller incorporation and centre pivot chemigation.

The aim of the study, test formulation, application rate (adjusted to equal required rate in the centre pivot sprinkler trial), recording of environmental and soil conditions, loader and applicator replicates, inhalation exposure measurement, physical examination of study participants, street clothes and preparation of field samples and control samples were as in Pan-Ag Study No EF-91-360, August 1993 (refer above for details).

Loaders and applicators wore long-sleeved shirts and long pants. In addition, loaders wore rubber boots, goggles, respirators and neoprene gloves. Applicators were provided with goggles, respirators and neoprene gloves to wear at their own discretion or when an odour was detected. Loaders transferred bulk metham using hose and couplers as in Pan-Ag Study No EF-91-360.

Charcoal air sampling filters were analysed for MITC and CS_2 by gas chromatography by Morse Laboratories Inc. The Morse Laboratories Inc. report is included in the submission but not commented upon further here. The Rosenheck report presents and comments on quality control data.

The MQL value for MITC and CS_2 is 1 μg.

<u>Rotary tiller trial - method and results</u>

The rotary tiller trial was conducted on previously cultivated bare ground and consisted of ten loader and ten applicator replicates. A loader replicate was taken as the time taken to load 100 gallons of metham. This ranged from 3-11 minutes, with geometric mean (GM ± SD) 7 ± 2.

The rotary tiller incorporated a 220 gallon capacity tank secured above a tool bar. Six blades (each fitted with six nozzles) were attached to the tool bar. Metham was applied only when the blades were in the ground at 38 psi. A large roller which sealed the soil was attached behind the tool bar.

All airborne CS_2 residues associated with loaders were below the MQL. GM ± SD of MITC residues were 0.787 ± 0.928 mg/hr (range 0.316 - 3.22 mg/hr) and 0.000323 ± 0.00027 mg/kg ai handled (range 0.000205 - 0.001095 mg/kg ai). A spill of metham occurred in one filling operation but this did not appear to influence airborne residues. The loaders wore goggles and respirators as part of normal personal protective equipment (PPE) requirements.

All application replicates used closed cabs, five with charcoal air filters and five with cellulose air filters. An applicator replicate was taken as application over one hour. This ranged from 56 - 72 minutes (GM 68 ± 5.1).

Airborne exposure and potential exposure incidents for applicators are given in Table 7. Applicators had higher exposure potential to MITC than CS_2 residues. Carbon disulfide residues were below the MQL for all workers. Potential inhalation MITC exposure was higher for applicators than loaders, when expressed as either mg/hr (GM 1.03) or mg/kg ai (GM 0.00393), at a minute volume of 29 L per minute.

The previous study in Arizona (Pan-Ag Study No EF-91-360) suggested that there was not much difference in MITC residues between open cabs and closed cabs with cellulose filters. In this trial, only closed cabs were used. Cellulose filters slightly out-performed charcoal filters but results were confounded as some cabin doors were open during the application time. Replicate 2 (charcoal filter) has high potential exposure, with no obvious reason cited.

Comments on worker incidents in Table 7 do not reveal any exposure incidents out of the ordinary. Two ground tillers noted odour, but only one of these (Replicate 2) has potential MITC exposure considerably above the mean.

Centre pivot sprinkler system- method and results

The centre pivot chemigation trial was conducted on dormant uncultivated alfalfa, and consisted of five loader and five applicator replicates. A loader replicate was taken as the time to load 100 gallons of metham. This ranged from 8 - 12 minutes (GM 10 ± 1.7). Applicator replicates covered 4 hours (range 224 - 241 minutes, GM 237 ± 6.51).

This trial utilised a full-sized centre pivot, comprising a 1200 foot boom with 72 nozzles, 14 feet above ground level. Metham was injected into the system at the centre pivot, pumped through via an injector pump and dispensed at 80 psi.

Loaders used a closed transfer system. They filled the three nurse tanks (capacity 1000-1500 gallons) located next to the centre pivot, from the bulk storage tank using a hose and couplers. When the required quantity of metham solution was in the nurse tank, the hose was disconnected. Some replicates filled the partially full nurse tank as well as another empty nurse tank.

At the beginning of each replicate, the applicator checked the injection flow rate from the injector pump. When one nurse tank was nearly full he would shut off the flow and open the next tank (both by flipping a lever). During most of the replicate the applicator sat in a car located 10-50 feet from the centre pivot, checking the flow rate about every half-hour.

Residues of CS_2 were not detectable for loaders or applicators handling metham via centre pivot chemigation.

MITC airborne residues and potential exposure incidents are reported on in Table 8.

Potential MITC exposure was higher for applicators than loaders when expressed as mg/ka ai handled (GM 0.000685 vs 0.0000560) but not mg/hr (GM 0.156 vs 0.354), at a minute volume of 29 L per minute. No extraordinary exposure incidents were reported for chemigation workers.

Comparisons between the two application methods indicate (GM mg/kg ai handled) higher MITC residues are associated with tillage than chemigation tasks, and with application rather than loading.

- Loaders (chemigation) - 0.0000560 ± 0.0000061 mg/kg ai handled
- Loaders (tillage) - 0.000323 ± 0.000270 mg/kg ai handled

- Applicators (chemigation) - 0.000685 ± 0.000154 mg/kg ai handled
- Applicators (tillage) - 0.00393 ± 0.00460 mg/kg ai handled

Soil and weather conditions were monitored. The second tillage field (tillage applicator replicates 5-10) had higher soil moisture than the first field (65% vs 51% field capacity). It is not possible to judge if this influenced MITC residue formation.

Table 7: Airborne MITC residues and potential exposure incidents when applying metham using rc

Replicate number (Rep), worker ID	Cab and filter type	Eye and respiratory protective equipment	Inhalation exposure to MITC (mg/kg ai handled)	Inhalation exposure to MITC (mg/hr)	Potential exposur
Rep 1: Worker D	Closed cab with charcoal air filter	Respirator	0.00557	1.15	Applicator left the next to a dripping and wore a respira
Rep 2: Worker D	Closed cab with charcoal air filter	Respirator	0.0176	4.35	Odour detected in
Rep 3: Worker D	Closed cab with charcoal air filter	None	0.00333	0.939	Door of cab was c
Rep 4: Worker D	Closed cab with charcoal air filter	None	0.00257	0.634	
Rep 5: Worker D	Closed cab with charcoal air filter	None	0.00171	0.435	
Rep 6: Worker F	Closed cab with cellulose air filter	None	0.00294	0.818	
Rep 7: Worker F	Closed cab with cellulose air filter	None	0.00133	0.394	
Rep 8: Worker F	Closed cab with cellulose air filter	None	0.00672	1.79	Worker cleaned o replicate
Rep 9: Worker F	Closed cab with cellulose air filter	None	0.00296	0.832	
Rep 10: Worker F	Closed cab with cellulose air filter	None	0.00797	2.13	
Geometric Mean (SD)			**0.00393 (0.00460)**	**1.03 (1.13)**	

Source: Rosenheck L (1993b) Worker Loader and Applicator Exposure from Field Applications of Metham-Sodium, Pan-Ag Sodium Task Force c/o ZENECA Ag Products.

Table 8: Airborne MITC residues and potential exposure incidents when applying metham using ce

Replicate number (Rep), worker ID	Eye and respiratory protective equipment	Inhalation exposure to MITC (mg/kg ai handled) (a)	Inhalation exposure to MITC (mg/h
Rep 1: Worker E	None	0.000624	0.143
Rep 2: Worker E	None	0.000591	0.136
Rep 3: Worker B	None	0.000994	0.228
Rep 4: Worker B	None	0.000580	0.131
Rep 5: Worker B	None	0.000711	0.161
Geometric Mean (SD)		**0.000685 (0.000154)**	**0.156 (0.036)**

Source: Rosenheck L (1993b) Worker Loader and Applicator Exposure from Field Applications of Metham-Sodium, Pan-Ag Sodium Task Force c/o ZENECA Ag Products.

(a) all CS_2 residues below MQL (1μ)
(b) No exposure incidents reported. No worker opted for goggles and/or respirator

Only summaries of the following studies conducted in The Netherlands were made available to Worksafe Australia by registrants of metham.

Exposure of Applicant to MITC during Soil Disinfection With Metham-Sodium in the Industrial Potato Area, Mulder A, Roosjen Ja, Dijksterhuis A.
and
Exposure of Applicants to MITC during Soil Disinfection in Bulbfields With Metham-Sodium, de Rooij M, Dijksterhuis A, van Aartrijk J.

These summaries do not include application rates, number of replicates or detailed results. The results could not be evaluated in the Risk Assessment, however the overall observations are valid for the Australian situation and listed below:

- In a previous study, it was found that drips from machines on headlands play a major role in airborne emissions of MITC. Hence, the machines used in this study had anti-drip systems fitted;
- The highest levels of MITC were almost always reached shortly after soil treatment;
- Contamination of sealed cabs traps MITC within the cab resulting in higher MITC levels inside cabs than outside;
- "Blowthrough" equipment on injectors limited exposure by emptying the injector pipes into the soil before lifting the machine as a whole. This prevents leakage of metham at ground level;
- The method of filling the injector had an effect on exposure levels. Using the "vacuum" system gave higher MITC readings in air than using the "pressurised" system;
- Exposure to MITC while filling injectors did not contribute significantly to total exposure; and
- In a few cases, high MITC levels were measured above metham storage tanks.

3.5 Occupational exposure studies - dazomet

There were no worker studies submitted for dazomet.

3.6 Degradation

Degradation of metham in soil

Metham is degraded rapidly and extensively in soil to MITC. Theoretically, 510 g metham (the concentration in most EUPs) is transferred to 231 g MITC. Estimates vary about the time taken for metham to degrade to MITC. Published information gives the time for a 50% loss of metham from 23 min to 4 days (Tomlin (Ed), 1994) and 0.5 - 50 days (Smelt et al., 1989). Registrants provided Worksafe Australia with unpublished studies concerning the rate of anaerobic and aerobic soil metabolism of metham (Burnett, 1987a, b). Under study conditions, metham applied to soil degraded rapidly under aerobic conditions, with a half-life of 23 min. Under both aerobic and anaerobic conditions, most of the metham applied to soil was recovered as MITC. Subsequent soil residues were extensively metabolised to carbon dioxide (CO_2) (16.5% applied metham dose at 60 days). Under experimental conditions, temperature and soil type did not influence the amount of metham converted to MITC (Smelt et al., 1974).

However, soil and environmental factors have been shown to influence the rate (and extent) of metham degradation in the field. The rate of breakdown increases with the organic matter and clay content in the soil, varying from 1 hour in moist loam to 5 hours in sand (Gurban et al., (undated); Smelt et al., 1974; Gerstl et al., 1977a). The conversion rate of metham to MITC was increased with an increase in soil temperature (Smelt et al., 1974), low moisture content (Gerstl et al., 1977a) and smaller soil particles. Such factors may not be evident in experimental studies.

Once formed, MITC tends to move upwards through soil. Leaching of MITC to lower soil depths could not be demonstrated in two unpublished studies (Stauffer Chemical Company, 1986 a, b), though it can be anticipated under certain conditions. For instance, with low ambient temperatures (eg <6°C), a temperature inversion can occur in the soil and MITC can diffuse into the lower warmer soil layers (BASF Aktiengesellschahft, 1989).

MITC is poorly adsorbed by soil particles (Gerstl et al., 1977a) and disappears both by volatilisation and degradation. Half-lives for MITC loss from soil vary widely, with estimates of 8-14 days (Smelt et al., 1974). Influencing factors include soil type and temperature (but not moisture) and microbial populations.

Soil frequently fumigated with MITC can experience less efficacious control of soil borne pathogens, because of accelerated MITC degradation by adapted microorganisms (Smelt et al., 1989).

When plastic sheeting is used to seal-in MITC fumes, the appropriate material should be used. Low density polyethylene (LDPE) is not recommended as it is highly permeable to MITC (Leistra et al., 1990).

Degradation of dazomet in soil

BASF provided data on the environmental breakdown of dazomet. Under aerobic conditions, the apparent half-life of dazomet was 13.64 hours. It was rapidly degraded to MITC and small amounts of CS_2 and CO_2 assumed to be produced by a different degradation pathway to that producing MITC (Hawkins et al., 1987).

Soil characteristics can influence the degradation of dazomet and production of MITC (Hormann et al., 1989). Dazomet degradation was slower in soils with lower moisture levels, while soil temperature, pH, moisture content, type and presence of peatmoss affected the rate of release and amount of MITC produced.

Degradation of metham applied in irrigation water

Metham is the most unstable in water at pH 5, with a half-life of 7.8 hours (Stauffer Chemical Company, 1985).

The breakdown of metham to MITC in soil when applied via irrigation water was studied by Gerstl et al. (1977b). Degradation was extremely rapid and followed first order kinetics. The degradation rate was influenced by the soil:water ratio. The concentration of metham applied played a role only at low water contents. The half-life of metham was several minutes, depending on both initial concentration and moisture content, while that of MITC was several days.

Gerstl (1977b) concluded that for optimal results from metham application, a balance must be obtained between the rapid breakdown of metham to MITC and the degradation of MITC to non-toxic compounds. Metham should be applied through irrigation water at a constant concentration as single pulse applications lead to pockets of high and low soil MITC.

3.7 Re-entry exposure - airborne MITC with dazomet in greenhouses

BASF submitted a study entitled “Determination of the Volatile Degradation Products of BASAMID GRANULAR in the Greenhouse Model Test, BASF Aktiengesellschahft, ZAX Analytical Laboratory, September 7, 1993”.

Airborne MITC and formaldehyde (volatile compounds formed from dazomet degradation in soil) were measured during the week after soil treatment in greenhouses.

Three scenarios were tested. In Trial 1, 2 m^2 of soil was treated at a rate of 40 g/m^2 (within Australian label rate). The granules were incorporated, the area moistened and enclosed with sheeting up to a height of one meter to prevent the air above the treated area mixing with the surrounding air. In Trial 2, the experiment above was repeated but the test area was covered with PE sheeting (25 μm thick). In Trial 3, the entire greenhouse soil area was treated as above and covered with PE sheeting. Air samples were obtained from 30 cm above the treated soil (Trials 1 and 2) and 1 meter above the covered soil (Trial 3). The tests were carried out while outside temperatures were high, which the study authors claim is likely to cause accelerated degradation of dazomet. Only MITC levels are considered in this report.

MITC residues were trapped in a silica gel adsorption tube, separated by gas chromatography and quantified using an atom emission detector. The determination limit for MITC was 0.01 mg/m^3.

In Trials 1 and 2, MITC concentrations increased rapidly within the first 20 hours after application, with and without sheeting. However, maximum concentrations were much higher without sheeting (maximum 43 mg/m^3 at 3 hours) than with sheeting (maximum 3.1 mg/m^3 at 1.5 hours). In both trials, MITC levels declined rapidly after 20 hours post application. In Trial 3, MITC levels peaked within 20 hours (maximum 4.6 mg/m^3 at 10 hours) and declined gradually (with occasional peaks) over the next 4-5 days. A small peak (1.2 mg/m^3) occurred when the sheeting was removed, but levels continued to decline. Airborne concentration of MITC remained at a level above that which caused ocular irritation in cats, 0.2 mg/m^3 (70 ppb), for approximately 72-96 hours (Trial 1), 24-48 hours (Trial 2) and 7 days including sheet removal at day 6 (Trial 3). This suggests that to avoid irritant effects of MITC after soil treatment in greenhouses with dazomet a re-entry period of 7 days is needed for unprotected entry. The use of PE sheeting contained about 90% of the peak airborne concentrations.

3.8 Field trip

A field visit was arranged in conjunction with a Pesticides Inspector from NSW, EPA, to observe soil fumigation with metham in a field situation in Mangrove Mountain and greenhouses in Maroota, NSW. Actual application of metham could not be viewed at either site, however discussions were held with the farmers and application equipment viewed.

Refer to Attachment A for details.

4. RISK ASSESSMENT

The Risk Assessment considers metham and dazomet exposure for workers involved in spraying/dispensing operations, when handling concentrates and working strength solutions. It further considers the exposure to product residues, in the form of MITC, for both re-entry workers and bystanders.

Workers handling metham products

Workers handling metham products, ie opening containers, pouring and measuring, may be splashed on skin and in the eyes. Metham is not volatile, hence inhalation exposure to metham vapour is not likely to be significant. Metham is stable in non-diluted aqueous solution, hence workers handling the concentrate should not be exposed to MITC.

Once diluted, metham is less stable and hydrolyses to MITC. The $t^1/_2$ for hydrolysis is 7-8 hours, in least stable conditions (Stauffer Chemical Company, 1985). Workers preparing the working strength solutions of metham will initially be exposed to metham. This may later be converted to MITC on the skin. During application of diluted metham products, workers may experience some skin contamination, which would be largely dependant upon the application method used. Spray mist may be generated during sprinkler applications. Applicators may be exposed to MITC vapour on the skin and through the respiratory tract, because as demonstrated in the Rosenheck studies and Mulder et al. (undated) and de Rooij et al. (undated) summaries (Section 3.4), metham may convert to volatile MITC during the application process.

Workers handling dazomet products

Workers handling dazomet granules will only be dermally exposed to the product. BASAMID GRANULAR is dust free. Dazomet has low vapour pressure. Hence, inhalation exposure to vapour or dust is not likely.

Given that dazomet granules are not mixed with water prior to application, workers applying the granules are not likely to be exposed to MITC, except as a result of simultaneous sealing (see below).

Post application exposure with metham and dazomet products

Workers involved in incorporating and sealing in metham or dazomet either during the application process or as a separate operation, can be exposed to MITC vapour. Similarly, bystanders may be exposed to MITC vapour if sealing is not immediate or is incomplete.

Workers re-entering treated areas may be exposed to MITC vapour if sealing is inadequate.

Workers and bystanders may also be exposed to other degradation products of metham, such as HS_2, CS_2, methylamine and N, N dimethylthiourea.

4.1 Dermal absorption

The extent of dermal absorption of metham, dazomet or MITC in humans or animals is not available, therefore assumptions are made.

The acute oral and dermal toxicity of MITC and metham are moderate. In the absence of dermal penetration studies for metham and MITC, the OHS report uses a default value of 10%.

A 21 day rabbit dermal study using dazomet was used in the Risk Assessment. Hence, a dermal penetration factor was not required for dazomet.

4.2 Acute toxic potential

The main acute hazards of metham are moderate dermal toxicity, corrosivity of skin, severe eye irritation and strong skin sensitisation. Dazomet is of low dermal toxicity and causes slight skin and eye irritation. The main hazards of MITC are moderate dermal and inhalation toxicity, severe skin irritation, corrosivity to eyes, respiratory irritation and moderate skin sensitisation.

Table 9: Theoretical quantities of product or spray required on the skin to reach the dermal LD_{50}

	Mixing/loading	**Application**
Metham	**Dermal exposure to metham-sodium** (a) (b) (c) • 76.4 mL undiluted product	**Dermal exposure to metham-sodium** (a) (b) (c) • 76.4 mL spray at 51% TGAC (d) • 3.9 L spray at 1% TGAC (e)
Dazomet	**Dermal exposure to dazomet** (f) (b) (g) • >123.7 g product	**Dermal exposure to dazomet** (f) (b) (g) • >123.7 g product

The following values were used in the above calculations:

(a) Dermal LD_{50} for metham-sodium 650 mg/kg
(b) Average body weight of a worker 60 kg
(c) Concentration of metham-sodium in all end use products 510 g/L
(d) Maximum concentration of metham-sodium in spray when used in seedbeds, lawns and limited areas, potting soil and field applications 51%
(e) Maximum concentration of metham-sodium in spray used in tobacco beds 1%
(f) Dermal LD_{50} for dazomet >2000 mg/kg
(g) Concentration of dazomet in end use product 970 g/kg

Table 9 estimates acute lethal volumes (corresponding to LD_{50}) for skin exposure of workers handling metham and dazomet products. For those handling product concentrates, the acute risk estimation assumes exposure to MITC is not involved. Dermal exposure less than 100 mL of undiluted metham is sufficient to reach the dermal LD_{50}. Applicators are less at risk, depending on the final working strength concentration of metham. Dermal exposure of >124 g of dazomet by loaders or applicators is needed to reach the dermal LD_{50}.

The acute dermal and inhalation toxicity plus the irritant effects of metham and MITC (detailed in Table 2), indicate that skin and respiratory protection is necessary for workers handling both concentrates and diluted spray. Workers independently sealing metham treated areas and those manually sealing in dazomet with water and covering the area with plastic will also need this protection.

It is not possible to quantify the acute risk for other workers or bystanders. Local conditions including application methods and effectiveness of sealing will influence volatilisation of MITC.

Metham is a dithiocarbamate compound. The acute toxicity of many dithiocarbamates can be increased by alcohol (Hayes WJ and Laws ER (Ed.) Handbook of Pesticide Toxicology, 1991).

Dazomet may be converted to MITC in contact with moist skin, hence skin protection is needed. Conversion of dazomet to MITC has been shown to be slower than with metham, hence respiratory protection is not warranted for activities other than manual watering and sealing with plastic.

4.3 Repeat dose toxic potential

Available information indicates that the same ground would not be treated with metham or dazomet more than 3 times per year, under Australian conditions. It is possible that certain categories of worker, eg. contract sprayers or those in the nursery industry, may handle the products more often.

Workers handling metham products

The only available NOEL for metham is 10 mg/kg/d established in developmental studies using rat (for maternotoxicity and foetotoxicity) and rabbit (for embryotoxicity). For a 60 kg worker, assuming 10% dermal penetration for metham, a daily dermal exposure of more than 6000 mg metham, 11 mL of undiluted product spray (at 51% metham) or 600 mL of the working strength metham spray (at 1% metham), is needed to exceed the NOEL. This calculation does not include a safety factor.

Repeated contamination with such volumes is not likely to be tolerated by workers because metham can induce severe irritant and/or sensitising effects with an exposure incident.

Workers handling dazomet products

The dermal NOEL of >1000 mg/kg/d, obtained from a 21 day rabbit study for systemic toxicity is used to assess the risk of repeated occupational exposure of workers using dazomet. Considering a 60 kg body weight, the equivalent daily dermal dose would be >60 g dazomet or >61.9 g BASAMID GRANULAR. This calculation does not include a safety factor.

Due to the formulation as granules, skin deposition of this quantity of product is not expected.

Exposure to MITC

It is possible that workers repeatedly handling either metham or dazomet may be exposed to MITC as a conversion product in metham solutions, from metham (or dazomet) breakdown on contaminated skin, or through environmental (airborne) exposure at application or when sealing treated areas.

The most appropriate NOEL for systemic effects of MITC is the inhalation NOEL from a 3 month rat study, of 30.7 mg/m^3 based on clinical signs. This is equivalent to 3.56 mg/kg (assuming a minute volume of 29 L/min, 4 hour exposure per day) for a 60 kg worker. The quantity of MITC generated from metham and dazomet will vary depending on environmental and other factors. Hence, it is not possible to provide an equivalent theoretical dose of metham or dazomet.

Topical effects have also been reported in workers routinely handling metham and dazomet in the workplace. These have been largely ascribed to the irritant and sensitising effects of MITC (Wolff and Jung, 1970; Schubert 1978; Richter, 1980). Therefore, workers repeatedly handling metham and dazomet need protection against irritant effects as well as any systemic effects.

4.4 Assessment of end use exposure studies

Metham/MITC

The risks of metham and MITC are considered as one. Toxic and topical effects resulting from exposure to metham/MITC are well documented. Irritation of eyes, nose and throat is associated with exposure to metham/MITC vapours and occurrences of contact dermatitis and/or skin sensitisation are reported following direct metham/MITC occupational exposure in the published literature. The reports on contact dermatitis and/or skin sensitisation largely deal with incidents of substantial exposure. It is highly likely that similar but less severe effects arising from minor exposures would not be reported to the same extent.

Threshold concentrations for metham/MITC for odour and irritancy were summarised in Table 3. However, from this data it is not possible to closely define concentrations applicable for humans. There is no regulatory exposure standard for MITC in Australia or via ACGIH, OSHA or NIOSH. These deficiencies, plus the fact that use pattern and environmental conditions strongly influence the degradation of metham to MITC, means that it is not possible to define acceptable occupational exposures to metham/MITC, particularly for irritant/sensitising effects. There is only limited information from occupational exposure studies that have monitored airborne MITC and any consequent worker health effects.

The studies of Rosenheck (1993a, b) have provided MITC airborne residues in mg/hr for metham loaders and applicators for both soil incorporation and chemigation uses. Airborne exposure, Margins of Exposure (MOE) and potential exposure incidents are in Table 10. In addition, estimated reference exposure limits of Alexeeff et al. (1994) are given in Section 2.6.

Table 10: Exposure to airborne MITC and margins of exposure for workers handling metham by soil incor

Task	Situation	No of transfers [1]	MITC mg/hr (29 LPM)	MITC mg/m^3 (29 LPM)	MOE [2]	MITC mg/kg ai handled	MITC mg/kg bw/day	MOE
Loader	Rotary tillage [4]	one [5]	0.787	0.45	68	0.000323	0.008 [6]	445
	Injection/rotary [7]	one [5]	0.775	0.45	68	0.000282	0.006 [6]	593
	Fixed sprinkler[7]	four [8]	1.50	0.86	36	0.00292	0.049 [9]	73
	Centre pivot [4]	six [10]	0.354	0.20	154	0.0000560	0.002 [9]	1780
Applicator	Rotary tillage [4]		1.03	0.59	52	0.00393	0.100 [6]	36
	Injection/rotary [7]		2.04	1.17	26	0.0109	0.231 [6]	15

	Fixed sprinkler [7]		2.60	1.49	21	0.0208	0.348 [9]	10
	Centre pivot [4]		0.156	0.09	341	0.000685	0.021 [9]	170

Source: Rosenheck (1993a, b)

(1) Transfer of metham from one tank to another during a discrete loading phase

(2) MOE = margin of exposure; 29 LPM is equivalent to 1.74 m^3/hr; NOEL = 30.7 mg/m^3 (three month rat inhalation study)

(3) MOE = based on the human dose equivalent to the NOEL derived from the three month rat inhalation study (30.7 mg/m^3

(4) Geometric mean

(5) Direct transfer from tanker to spray tank

(6) Kg ai handled for loaders and applicators is determined for the maximum Australian label rate for field crops of 255 treated in the studies. For rotary tillage: 275 kg ai (amount applied over one hour) x 8 hours = 2200 kg @ 356 kg ai per hect hectare = 1530 kg ai per day. For soil injection: 226 kg ai (amount applied over one hour) x 8 hours = 1808 kg @ 356 kg ai kg ai per hectare = 1275 kg ai per day. Average worker weight is 60 kg

(7) Arithmetic mean

(8) Transfer from tanker to mobile holding tank to nurse tank; operation repeated once

(9) Australian labels do not specify the amount of metham to be applied per hectare by linear or centre pivot systems. determined as two 4 hour chemigation applications per day at application amounts as given in each study (fixed sprinkler 900 kg ai, 1800 kg ai). Average worker weight is 60 kg. It is recognised that sprinkler capacity and design and work pattern

(10) Transfer from tanker to three nurse tanks; reported as six operations

For loaders, the MITC mg/hr, converted to mg/m^3, ranges from 0.2-0.86 mg/m^3, at or greater than the lowest irritant threshold of 0.2 mg/m^3 (in cats). Potential airborne MITC exposure for all loaders would exceed the Alexeeff et al. (1994) reference exposure limit for preventing discomfort (0.0014 mg/m^3), and one (loaders for fixed sprinklers) would exceed the limit for preventing life threatening effects (0.488 mg/m^3). However, the true impact on workers is uncertain as loaders would handle metham only intermittently throughout the day. The loaders in the study wore respirator and goggles and no breakthrough odour or irritation was reported. As a precaution, a respirator and goggles would be warranted. MOE for loaders without respirators are calculated from mg MITC/kg metham handled under the equivalent Australian use pattern and the inhalation NOEL for MITC systemic toxicity of 30.7 mg/m^3, equivalent to 3.56 mg/kg bw/d (for a 60 kg worker), for the four loader groups, all using enclosed transfer systems. MOE range from 73 - 1780. There were small metham spillages inherent in the transfer operation and occasional more substantial spills. The more substantial spills did not appear to influence MITC exposure. Dermal exposure was not measured.

Airborne exposure in mg/hr, converted to mg/m^3, may be more applicable to applicators who are handling metham over extended periods. Workers applying metham to soil by injection and/or rotary tillage were protected by engineering controls, closed cabs with air filters or, if in open cabs, by respirators. The range of MITC outside the respirators was 0.22-3.86 mg/m^3. Breakthrough odours were reported on two occasions in closed cabs (MITC = 0.66 mg/m^3 and 2.5 mg/m^3). On occasions where no odour was reported, MITC in cabs ranged from 0.17-1.79 mg/m^3. Workers applying metham from open cabs and wearing respirators did not report any odours. For all applicator groups, except those dealing with centre pivot irrigation, the mean MITC mg/m^3 was greater than the Alexeeff et al. (1994) limit for preventing life threatening effects (0.488 mg/m^3). The group most at risk was the fixed sprinkler applicator group (MITC = 1.49 mg/m^3), that experienced the most severe fuming episodes. Again, it is not possible to define threshold concentrations for airborne residues. Results suggest however, that the integrity of the engineering controls, filters and sealing of the cabin (including vacating the cabin when performing running repairs to equipment), is important in excluding vapours. There was a suggestion in these studies that charcoal and cellulose filters may alter in the degree of protection afforded. This requires further investigation as a lesser degree of protection may be experienced than for workers in open cabs but wearing respirators and goggles. This is supported by the observations of Mulder et al (undated) and de Rooij et al (undated) that contamination of sealed cabs traps MITC resulting in higher levels inside than outside.

The Rosenheck (1993a, b) studies investigated direct soil injection and rotary tillage incorporation of metham. Results were insufficient to conclude any differences between the application techniques. Mulder et al (undated) and de Rooij et al (undated) reported that anti-drip devices in particular and “blowthrough” soil injectors would reduce metham leakage and MITC emissions.

MOE for soil applicators are calculated from mg MITC/kg metham applied and the dose equivalent to the inhalation NOEL for metham systemic toxicity, for a 60 kg worker. They are substantially lower than for loaders (36 and 15, rotary tillage and injection, respectively), and are associated with applications where fuming was obvious. Dermal exposure for applicators was not measured.

In the Rosenheck (1993a, b) studies, airborne MITC levels during chemigation were associated with both the irrigation technique (ie the tasks requiring entry into treated areas by workers) and prevailing wind conditions. Both these factors resulted in workers dealing with metham application via fixed sprinklers experiencing fumes and some considerable discomfort. Airborne MITC levels with fixed sprinklers were 1.49 mg/m^3. Under the trial conditions, metham application via centre-pivot irrigation resulted in lower MITC concentrations, mean of 0.09 mg/m^3: Inhalation exposure converted to an equivalent dose for a 60 kg worker resulted in MOE of 10 and 170 for fixed sprinkler applications and centre-pivot irrigation respectively.

Based on the results from the Rosenheck (1993a, b) chemigation studies, it is not possible to recommend any particular type of overhead sprinkler technique over another, because wind conditions during the fixed sprinkler trial caused excessive fuming. However, the data does indicate that techniques must not involve workers remaining to perform tasks where MITC fumes are to be expected irrespective of weather conditions on the day. The use of respirators and goggles during the entire application process is not considered to be a practical option as application may require several hours.

No information was available to assess the use of metham through trickle irrigation systems or flood irrigation. However trickle irrigation allows both low volume metham use and enclosed application under plastic sheeting. Neither of these conditions apply with metham application by flood irrigation.

Metham/CS_2

In the Rosenheck (1993a, b) studies above, CS_2 was below the MQL in most samples, and where detected, never approached the NOHSC exposure standard of 31 mg/m^3 (TWA).

Dazomet/MITC

No end use exposure studies for dazomet/MITC were available for assessment. A re-entry air residues study is assessed in Section 4.7

4.5 Assessment using exposure calculation models

4.5.1 Predictive Operator Exposure Model (POEM) - metham and dazomet

Worksafe Australia did not use the exposure calculation model POEM to extrapolate end user exposure to metham, dazomet or MITC, as it does not simulate the application methods.

4.5.2 German operator risk assessment - dazomet

BASF, the registrant of BASAMID GRANULAR, provided an estimation of operator exposure to dazomet based on the German Operator Risk Assessment Model (BASF Reg. Doc. 95/10731), while acknowledging that this model is not designed for soil fumigation.

The BASF exposure estimation assumes that dermal and inhalation exposure is carried by the dust portion of the granular formulation (0.8% of the product), and uses the inbuilt model parameters for powders (particles <100μ). No justification for this is provided. However, accepting the estimates for dermal and inhalation exposure and utilising the 21 day dermal NOEL of 1000 mg/kg bw/d (rabbit) and the subchronic oral NOEL of 0.8 mg/kg bw/day (dog), MOE can be calculated for mixer/applicators. The scenario uses maximum label rates of 680 kg product/ha, tractor treatments of 1 ha/day and hand-held treatments of 0.05 ha/day, as provided in the BASF submission. It is not an unreasonable scenario for dazomet use under Australian conditions.

MOE obtained for tractor treatments are 1380 and 123, dermal and inhalation respectively. MOE obtained for hand-held treatments are 2560 and 162, dermal and inhalation respectively. Despite the limitations inherent in the above extrapolations, exposure margins suggest systemic toxicity caused by dazomet alone should not occur under normal use conditions.

This assessment does not consider any subsequent exposure to MITC.

4.6 Conclusions on operator exposure

<u>Metham/MITC</u>

There is no information on the extent of health effects, such as contact dermatitis and dermal or respiratory sensitisation among workers handling metham in Australia.

Worker protection (engineering controls and PPE) is needed to prevent skin irritation and/or skin sensitisation resulting from contamination with spills of metham solutions (all concentrations).

No data was available to assess dermal exposure, for any registered metham use, hence MOE for dermal exposure could not be estimated. However, the severity of metham/MITC topical effects is such that workers are unlikely to allow themselves to regularly experience skin contamination to amounts greater than the NOEL for repeat dose toxicity (equivalent to 11 mL undiluted product). Worker protection (engineering controls and PPE) is needed to protect against dermal contamination of metham in all registered uses.

Exposure models - POEM is not applicable to the metham use pattern and was not used.

Worker studies on MITC airborne exposure indicate that workers loading metham using enclosed transfer systems, may be subjected intermittently to MITC above the irritant threshold and in circumstances that cannot be defined. These workers require respiratory and eye protection.

There was no data on airborne MITC for open transfer systems, any metham dilution activities or transfer by chemical probe (the method observed on the metham field visit).

Worker studies on MITC airborne exposure during soil applications indicate that residues are influenced by the integrity of engineering controls, such as air filters in tractor cabs and modifications to application equipment to reduce metham drips. Users, chemical retailers and equipment builders/sellers need to be provided with advice on engineering controls for metham, to avoid a trial and error approach by users.

It is logical to surmise that direct soil injection would result in lower airborne residues than spraying on the soil surface followed immediately by soil incorporation. In the studies presented, results were confounded by variable efficiency in cab filter types. Therefore ultimately there was insufficient information to conclude that soil injection would be superior due to the other varying influences on exposure.

Worker studies on MITC airborne residues during centre-pivot and sprinkler irrigation indicated that airborne residues, fumes, operator discomfort and MOE were related to operator tasks and prevailing wind conditions. The practicality of operators wearing sufficient protective equipment, respirator and goggles, during the entire application time is questioned. There is insufficient information to ascertain if the donning of respirator and goggles when odour is detected, provides sufficient protection against irritant effects or systemic toxicity.

No data is available to assess worker exposure when using trickle irrigation systems or during flood irrigation. However it is feasible for trickle irrigation to occur in a controlled manner, but not flood irrigation.

Metham (other situations and methods) - No worker exposure data was available for assessment for seed beds, lawns and limited areas - all uses; field application (beds and rows) - trickle irrigation, soil covering method; potting soil - all uses and tobacco plant beds- all uses.

Dazomet/MITC

There is no information on the extent of health effects, such as contact dermatitis and dermal or respiratory sensitisation among Australian workers handling dazomet.

Worker protection is needed to minimise the skin irritation of dazomet granules. In addition, skin protection is required to minimise dermal toxicity and skin irritation and/or sensitisation of MITC, that may form when dazomet comes in contact with moist skin.

The granular formulation of BASAMID GRANULAR is not conducive to significant skin contamination, providing appropriate clothing prevents trapping of granules next to the skin.

Exposure models - POEM is not applicable to the dazomet use pattern and was not used.

Exposure models - BASF submitted an extrapolation of the German Operator Risk Assessment Model as an estimate of operator inhalation and dermal exposure to dazomet. The MOE calculated based on the systemic toxicity of dazomet, indicate that exposure to the powder component of the granules does not introduce a significant risk.

There is no measured worker exposure data for airborne MITC residues released upon dazomet reaction with moist soil or sealing-in water, during or immediately after application, in sites other than greenhouses. Workers manually sealing with water and laying plastic sheeting will require respirators and goggles, to protect against exposure to airborne MITC.

In greenhouses, airborne MITC above watered-in dazomet-treated soil was 5.1 mg/m^3 at the first time point of 25 minutes after sealing. This value far exceeds the minimum irritant threshold of 0.2 mg/m^3 (in cats) and a derived human reference exposure limit (0.0014 mg/m^3). This suggests that workers performing manual water-sealing plus subsequent plastic sealing in greenhouses require respirators and goggles.

4.7 Personal protective equipment indicated by the risk assessment

The personal protective equipment required to protect end users against health effects following acute and repeated exposure is given in Tables 11 and 12.

Table 11: Personal protective equipment required in Safety Directions for Metham resulting from acute and repeat dose risk assessment

Risk assessment	Personal protective equipment (tasks)
Acute risk Section 4.2	
• acute lethal dermal toxicity (metham and MITC)	elbow-length (nitrile, neoprene) gloves, cotton overalls buttoned to the neck and wrist, a washable hat (when opening containers, preparing and applying spray). In addition, chemical resistant apron (when opening containers and preparing spray)
• acute lethal inhalation toxicity (metham and MITC)	full facepiece respirator with organic vapour/gas cartridge or canister [or goggles and half facepiece respirator with organic vapour/gas cartridge or canister] (when opening containers, preparing and applying spray).
• eye irritation (metham and MITC)	full face respirator or goggles (when opening containers, preparing and applying spray).
• skin irritation (metham and MITC)	cotton overalls buttoned to the neck and wrist, elbow-length (nitrile, neoprene) gloves, chemical resistant footwear, chemical resistant apron (when opening containers, preparing and applying spray).
• skin sensitisation (metham and MITC)	as for skin irritation
Repeat dose risk	
• worker study Section 4.4 (systemic toxicity)	respirators and goggles (when opening containers, preparing spray and applying spray).
• repeat dose toxic potential Section 4.3	as for acute risk

Table 12: Personal protective equipment required in Safety Directions for Dazomet resulting from acute and repeat dose risk assessment

Risk assessment	Personal protective equipment (tasks)
Acute risk Section 4.2	
• acute lethal dermal toxicity (dazomet and MITC[1])	cotton overalls buttoned to the neck and wrist, elbow-length (nitrile, neoprene) gloves, chemical resistant footwear (when opening containers and using the product)
• acute lethal inhalation toxicity (dazomet[2])	nil
• eye irritation (dazomet[2])	nil
• skin irritation (dazomet and MITC[1])	cotton overalls buttoned to the neck and wrist, elbow-length (nitrile, neoprene) gloves, chemical resistant footwear (when opening containers and using the product)
Repeat dose risk (exposure plus systemic health effects)	
• German Operator Risk Assessment Section 4.5.2	nil
• repeat dose toxic potential Section 4.3[2]	elbow-length (nitrile, neoprene) gloves, cotton overalls buttoned to the neck and wrist (when opening containers and using product)

1 - Considers the conversion of dazomet to MITC when in contact with moist skin
2 - The toxicity of MITC was not considered because the conversion of dazomet to MITC is not likely to be rapid and the product is not mixed with water prior to application

PPE requirements in Tables 11 and 12 are consolidated in the Safety Directions for metham and dazomet products in Section 6.6.

4.8 Immediate post-application entry and re-entry assessment

For agricultural uses, metham and dazomet are expected to degrade extensively to MITC, with faster degradation for metham than dazomet. The speed and extent of degradation of MITC and the products formed are dependent upon soil type, environmental conditions (particularly soil temperature) and agricultural application methods.

Immediate post-application entry-metham

There is little information available upon which to quantify specific risks to individual workers who may only perform the task of sealing in the site (ie. watering or laying plastic sheeting). Mulder et al (undated) and de Rooij et al (undated) observed the highest MITC almost always shortly after treatment. Risks to these workers in exposure to MITC airborne residues will be at least as great as those for applicators, and may be increased as more MITC is formed over time. Anecdotal evidence obtained during the metham field visit suggested that the plastic sealing operation was associated with substantial discomfort when adequate PPE was not used.

Considering these factors, it will be appropriate for workers separately involved in the sealing-in of metham products to wear the same protective clothing as that specified for metham product applicators.

Immediate post-application entry - dazomet

Workers separately performing manual water-sealing and plastic sealing for dazomet granules in greenhouses or in the open will need the PPE specified for dazomet applicators plus a respirator and goggles, to protect against rapidly forming MITC.

Re-entry into treated areas

There is little information upon which to base a particular restricted entry interval for workers. Metham itself may degrade quickly, forming MITC. The amount of airborne MITC depends both upon application methods (ie. soil injection or surface spraying), the timeliness and effectiveness of the sealing process and prevailing environmental conditions.

The BASF dazomet greenhouse studies indicate that maximum levels of MITC occur within the first 24 hours after treatment, then levels gradually decrease. Similarly, the summaries of studies by Mulder et al (undated) and de Rooij et al (undated), stated that the highest MITC residues are found soon after soil treatment with metham.

Considering all the above, Worksafe Australia recommends the following re-entry periods be specified on product labels.

Metham and dazomet products:

Re-entry period - field uses
Do not allow entry into treated areas for 48 hours. When prior entry is necessary, wear personal protective equipment specified for applicators. Clothing must be laundered after each day's use.

Metham products:

> **Re-entry period - greenhouse application, including under plastic**
> Do not allow entry into treated areas for 7 days. When prior entry is necessary, wear personal protective equipment specified for applicators. Clothing must be laundered after each day's use. Thoroughly ventilate greenhouses for 24 hours after removing plastic.

Dazomet products:

> **Re-entry period - greenhouse application, including under plastic**
> Do not allow entry into treated areas for 7 days. When prior entry is necessary, wear personal protective equipment specified for applicators with goggles and a half face respirator with organic vapour/gas cartridge. Clothing must be laundered after each day's use. Thoroughly ventilate greenhouses for 24 hours after removing plastic.

A re-handling period is needed for treated potting soil. The following statement should appear on metham and dazomet product labels.

> **Metham-sodium - potting soil:**
> Treated soil is to remain covered by plastic sheeting or similar material impermeable to MITC, for 7 days after treatment. When prior handling is necessary, wear personal protective equipment specified for applicators. Clothing must be laundered after each day's use.

> **Dazomet - potting soil:**
> Treated soil is to remain covered by plastic sheeting or similar material impermeable to MITC, for 7 days after treatment. When prior handling is necessary, wear personal protective equipment specified for applicators with goggles and a half face respirator with organic vapour/gas cartridge. Clothing must be laundered after each day's use.

It is not possible to comment extensively on bystander exposure as a result of information provided for this assessment. Instances of irritant effects in bystanders have been documented earlier in this report. The escape of MITC residues to the air is dependent on the effectiveness of agricultural operations, including the sealing process. These may in turn be influenced by environmental conditions, such as soil factors promoting more rapid conversion to MITC and prevailing wind for drift. The importance of site and weather conditions, as opposed to sole consideration of distance from the source of MITC, was highlighted in the study of human health effects following the Sacramento River spill (Cone et al., 1994; Kreutzer et al., 1994). The investigations by these authors could not help define boundaries of buffer zones. Users need to be provided with advice on the best agricultural methods required to minimise exposure to bystanders (as well as operators).

5 REGULATORY CONTROLS

5.1 Statement of hazardous nature

Metham, dazomet and all the end use products are determined to be hazardous substances according to NOHSC criteria. Hazardous substances are subject to the workplace controls outlined in the NOHSC Control of Workplace Hazardous Substances (NOHSC, 1994b).

5.2 Exposure standards

National Occupational Health and Safety Commission (NOHSC) exposure standards have not been assigned for metham, dazomet or MITC (NOHSC, 1995).

Carbon disulfide has a NOHSC exposure standard of 10 ppm or 31 mg/m^3 (TWA) with a skin notation. Hydrogen sulfide has a NOHSC exposure standard of 10 ppm or 14 mg/m^3 (TWA) and 15 ppm or 21 mg/m^3 (STEL).

6. WORKSAFE AUSTRALIA RECOMMENDATIONS TO THE NRA

Metham sodium and dazomet

Advice on compliance issues has been sought from RLC members and considered in developing the Recommendations.

6.1 Exposure standards

Worksafe Australia proposes that the NOHSC Exposure Standards Expert Working Group consider setting an exposure standard for MITC.

Rec (1) The NRA release the Worksafe Australia OHS Technical Report Metham-Sodium, Dazomet, Methylisothiocyanate (1997), the TGA Toxicology Reports (1995, 1996) and the worker exposure data submitted for this review, to the NOHSC Exposure Standards Expert Working Group.

6.2 Uses - metham sodium

Existing uses of metham sodium are supported, subject to restrictions on hand directed spraying (Rec 2), treatments of potting soil (Rec 3), irrigation applications (Rec 4) and tobacco plant bed applications (Rec 5).

Rec (2) Hand directed spraying, including Sprinkler can treatment is not supported.

Rec (3) Potting soil Treatment of potting soil is supported only when restricted to treatment via an enclosed potting mixer in a well ventilated area. Treated soil is to be covered by plastic sheeting or similar material impermeable to MITC. Treatment of loose mixed soil or via a shredder is not supported.

Rec (4) Irrigation application Irrigation treatment is supported only when applied via trickle irrigation under plastic sheeting, in greenhouses or fields. Application by flood irrigation or overhead sprinkler systems is not supported.

Rec (5) Tobacco plant beds Tobacco treatment using hand directed methods is not supported, in accordance with Rec (2).

The above restrictions must be specifically prohibited on labels to ensure they are not allowed under some state control of use regimes.

6.3 Uses - dazomet

Existing uses of dazomet are supported.

6.4 Training and information provision; restriction on availability - metham sodium and dazomet

Training is essential to minimise on-site and off-site effects of volatile degradation products. Training must cover the general aspects of chemical handling plus the specific requirements of MITC-generating chemicals. Sources of information and relevant topics for educational material concerning these specific requirements are provided in Attachment B.

Technical plus exposure information available for review did not allow Worksafe Australia to make recommendations on equipment type and design features, specifically for mixing/loading, tillage applications and filter types for enclosed cabs. This information is important for equipment designers and makers, to provide equipment that dispenses metham-sodium in particular, under optimal conditions that minimise exposure to workers.

Material safety data sheets are required for all existing metham sodium and dazomet products. The limited numbers submitted for the review need upgrading to meet NOHSC requirements.

Rec (6) Specific training in the use of metham sodium and dazomet products is required. The NRA request Farm Chemicals Users Course organisers to determine whether the training should be incorporated in the Farm Chemicals Users Course, a specific fumigation module or other short specific module. Facts Sheets are to provide written technical reference material for trainers and users (see Rec 7). The NRA needs to ensure a mechanism exists for this training requirement, if necessary by scheduling metham and dazomet as restricted chemical products by regulation.

Rec (7) The NRA require registrants to compile product Fact Sheets, concerning the safe use of these chemicals for users and bystanders. All Fact Sheets should be submitted to Worksafe Australia for assessment to ensure they are of consistent quality. Advice from RLC members may be needed at this stage. Fact Sheets should be made available to users via the Farm Chemicals Users Course or specific module and the point of sale; they should be provided to equipment manufacturers/sellers and chemical retailers by the registrants. Technical fact sheets and brochures already developed by some registrants could form the basis of new sheets.

Rec (8) The NRA seek advice from RLC members about sources of technical information on equipment type and design features, for tillage or other types of application of metham-sodium in particular and preferred filter types for enclosed cabs, with at view to enabling end users to minimise uncontrolled exposure and MITC emissions. This information is to be included in the Fact Sheets.

Rec (9) The NRA advise all registrants that all product material safety data sheets are to be amended to meet NOHSC requirements and submitted to Worksafe Australia for assessment.

6.5 Safety Directions

Metham and MITC have similar toxicological profiles, with MITC exhibiting more severe effects upon inhalation and contact with the skin and eyes. Dazomet is less acutely toxic, less irritant and non-sensitising. The safety directions for metham take into account that MITC may also be present, in undefined amounts. As the product formulations and use patterns are different between metham products (liquids) and the dazomet granular product separate safety directions are recommended.

Safety directions are agreed between the TGA and Worksafe Australia.

<u>Metham-sodium SC 510 g/L or less</u>

129 131 133	Harmful if absorbed by skin contact or swallowed
130 132	Poisonous if inhaled
207 162 163 164	Will damage the eyes, nose and throat and skin
180	Repeated exposure may cause allergic disorders
204	Interacts with alcohol
220 222 223	Do not inhale vapour or spray mist
240	The fumes first cause smarting, then watering of eyes. This should be taken as a warning sign
260	The liquid can cause burns

271	Use and store in well ventilated areas.
279 280 281 290 292 293c 295 298a 301 307 [or 297 300 307]	When opening the container and preparing product for use, wear cotton overalls buttoned to the neck and wrist, a washable hat, apron (chemical resistant), elbow-length (nitrile, neoprene) gloves, chemical resistant footwear, a full facepiece respirator with organic vapour/gas cartridge or canister [or goggles and half facepiece respirator with organic vapour cartridge or canister]
279 282 290 292 295 298a 301 307 [or 297 300 307]	When using the prepared (spray) (foam), wear cotton overalls buttoned to the neck and wrist, a washable hat, elbow-length (nitrile, neoprene) gloves, chemical resistant footwear, a full facepiece respirator with organic vapour/gas cartridge or canister [or goggles and half facepiece respirator with organic vapour cartridge or canister]
330 331 332	If clothing becomes contaminated with product or wet with spray, remove clothing immediately
340 341 342	If product or vapour on skin, immediately wash area with soap and water
340 341 343	If product or vapour in eyes, wash it out immediately with water
350	After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water
360 361 363 364 366 370	After each day's use, wash gloves, goggles, respirator and if rubber wash with detergent and warm water and contaminated clothing. Do not re-use footwear until thoroughly aired

<u>Dazomet GR 980 g/kg or less</u>

120 130 133	Product is poisonous if swallowed
161 162 163 164	Will irritate the eyes, nose and throat and skin
210 211	Avoid contact with eyes and skin
220 221	Do not inhale dust

240	The fumes first cause smarting, then watering of eyes. This should be taken as a warning sign
279 280 283 290 292a 295 298a	When the opening container and using the product, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) elbow-length (nitrile, neoprene) gloves and chemical resistant footwear
340 342	If product on skin, immediately wash area with soap and water
350	After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water
360 361 366 370	After each day's use, wash gloves and contaminated clothing. Do not re-use footwear until thoroughly aired

6.6 Product labels

Rec (10) Reference to the MSDS All metham sodium and dazomet products are hazardous substances and require a reference to the MSDS on the label.

Rec (11) The following label precaution statements are required. They should be located directly under the safety directions.

Metham-sodium and dazomet products:

> Workers previously experiencing skin or respiratory tract irritation from metham-sodium or dazomet exposure should not work with metham-sodium or dazomet products.

Metham-sodium products:

> After mixing with water do not allow mixture to stand as poisonous fumes are released on standing.
>
> Workers manually sealing should wear the personal protective clothing specified for applicators.

Dazomet products:

> Workers performing manual water-sealing and plastic sealing should wear the personal protective clothing specified for applicators plus a respirator with organic vapour/gas cartridge and goggles.

Rec (12) The following re-entry statements are required on product labels. They should be located directly under the safety directions.

Metham-sodium and dazomet products:

Re-entry period - field uses
Do not allow entry into treated areas for 48 hours. When prior entry is necessary, wear personal protective equipment specified for applicators. Clothing must be laundered after each day's use.

Metham-sodium products:

Re-entry period - greenhouse application, including under plastic
Do not allow entry into treated areas for 7 days. When prior entry is necessary, wear personal protective equipment specified for applicators. Clothing must be laundered after each day's use. Thoroughly ventilate greenhouses for 24 hours after removing plastic.

Dazomet products:

Re-entry period - greenhouse application, including under plastic
Do not allow entry into treated areas for 7 days. When prior entry is necessary, wear personal protective equipment specified for applicators with goggles and a half face respirator with organic vapour/gas cartridge. Clothing must be laundered after each day's use. Thoroughly ventilate greenhouses for 24 hours after removing plastic.

Rec (13) The following re-handling statements are required on product labels. They should be located directly under the safety directions.

Metham-sodium - potting soil:
Treated soil is to remain covered by plastic sheeting or similar material impermeable to MITC, for 7 days after treatment. When prior handling is necessary, wear personal protective equipment specified for applicators. Clothing must be laundered after each day's use.

Dazomet - potting soil:
Treated soil is to remain covered by plastic sheeting or similar material impermeable to MITC, for 7 days after treatment. When prior handling is necessary, wear personal protective equipment specified for applicators with goggles and a half face respirator with organic vapour/gas cartridge. Clothing must be laundered after each day's use.

6.7 Overseas reviews

The US EPA is awaiting and reviewing data on metham, dazomet and MITC. In accordance with standard practice, the US EPA report will be considered when available. Additional data which may have been available will be identified and if necessary, advice on the implications will be provided to the NRA.

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WORKSAFE AUSTRALIA
OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

ATTACHMENTS

NAME OF PRODUCT:	SEVERAL PRODUCTS
ACTIVE INGREDIENT:	METHAM-SODIUM DAZOMET METHYLISOTHIOCYANATE
NAME OF APPLICANT:	SEVERAL
DATE OF THIS REPORT:	5 August, 2000
WORKSAFE AUSTRALIA FILE NO:	94/0843
NRA FILE NO:	G01268 and G01269
ATTACHMENT A:	Report on metham field trip
ATTACHMENT B:	Relevant topics for educational material concerning specific requirements for MITC-generating chemicals Sources of information

Attachment A

FIELD VISIT TO A HORTICULTURAL PROPERTY AND GREENHOUSE IN NSW - METHAM USAGE

A field visit was arranged in conjunction with a Pesticides Inspector from NSW, EPA, to observe soil fumigation with metham in a field situation in Mangrove Mountain and greenhouses in Maroota, NSW, on Tuesday 17 September 1996. Actual application of metham could not be viewed at both sites, however discussions were held with the farmers and application equipment viewed.

Field crop (carrots)

The owner of the carrot crop was an experienced metham user who had been using the product for several years without any problems. He used the product mainly to control nematodes and considers it a very effective nematicide. He rotated the carrot crop with a fibrous root crop, such as lettuce. The farmer predicted the requirement for soil treatment for his next crop, by observing the roots of the current crop of carrots or lettuce (at harvest) for evidence of nematode damage, ie knotting of roots. If nematode damage was evident, he would treat the soil with metham prior sowing the next carrot crop. In general, he used metham approximately once per year with application taking place around March. The farmer is of the opinion that metham should act within the first 24 hours, to be effective.

The owner carried out all metham applications himself. He only used soil injection equipment and does not believe that other application methods are as efficacious. His equipment consisted of seven tynes (alternating 4 in front and 3 behind, to ensure that the whole area was treated). Each tyne had a hose and nozzle attached behind it, which delivered the metham into the soil. The soil injection equipment also contained an oblong metal bar attached behind the second row of tynes, which compacted the soil after it was treated. The farmer indicated that he had used a roller in place of the metal bar, but found it collected dirt and was ineffective.

The farmer was aware of the need to maintain adequate soil moisture before metham treatment. If the soil was too dry, he would water it using the sprinklers.

He carried out metham treatment in the latter part of the day. He only handled 200 L containers. Metham was used undiluted and applied at label rates. Preparation of the equipment and loading the drums was carried out in a large machinery shed near the field. A typical application sequence would be: loading the 200 L drum onto the injection equipment and anchoring it with chains, inserting the chemical probe (which extends to the bottom of the drum) through the opening at the top of the drum, attaching the equipment to the open tractor and driving to the field. Once the equipment was positioned in the field, the tynes are inserted into the ground before the metham delivery is commenced. The delivery system is turned off before the tynes are lifted out of the ground at the end of each row. He did not water in the metham but relied on the dew fall for this action. He was able to treat one hectare in approximately 20 minutes.

After a day's spraying, he would rinse the empty drums, collect the rinsings into one drum (using a funnel) and go through the field applying the rinsate to the soil. This also serves to flush out the equipment.

The farmer only used rubber gloves when loading the drum onto the soil injector and carrying out maintenance work on the equipment. He wore shorts and singlet with no other body covering. He had never experienced any odour or suffered irritant effects.

After soil treatment, the farmer did not go into treated areas for approximately 14 days, when he used a bed shaper to cultivate the soil and form the beds. He did not report suffering any irritant effects or noticing any odours during re-entry and cultivation. He did not carry out a germination tests prior to putting down the next crop.

Carrots are harvested mechanically.

Greenhouse crops (hydroponic tomatoes)

The owner of the greenhouses had used metham for several years to control nematodes and other soil borne pathogens. Due to problems with pathogen control, he has now shifted to substitute soil methods that do not require fumigation.

Metham use

Water for irrigation was obtained from a dam at the edge of the property. An open shed built near the dam contained a pump, drums of metham (200 L) and other mixing and loading equipment. Water and metham solution were delivered to the greenhouses via pipelines. Following is a typical sequence of events when applying metham via sprinkler or drip irrigation: the required quantity of metham solution was measured using a measuring jug and poured it into an open drum; water alone was pumped over or into the prepared beds for approximately 0.5 hours: the water was then directed into the drum containing metham at a preset rate and mixing was automated; the dilute metham solution was automatically pumped in through the drippers; water alone was applied at the end to clean out the application equipment. Empty drums were rinsed and added into the mixing drum.

The farmer wore overalls buttoned to the neck and wrist, elbow-length PVC gloves and boots. The description of work practices confirmed the belief that workers mixing/loading metham could be exposed to the solution.

Immediately after sprinkler application, he would lay down overlapping rows of plastic sheeting over each of the prepared seed beds, running the length of the greenhouse. The sheeting was held down at both ends by digging a shallow drain into which the edges were inserted and drains re-filled with soil. He estimated that it took approximately 10-15 minutes to cover each greenhouse. During this process, he often suffered irritation of the eyes, nose and throat and noticed an odour. This method of metham application is not carried out on this farm anymore.

In the drip irrigation system, the farmer re-entered the greenhouses and manually made small holes in the plastic sheeting, at the point of the drippers, after an interval of approximately 10 days, to release any residual fumigant and subsequently plant the seedlings. He has not noticed an odour or suffered irritant effects during this process. He never carried out germination tests.

Attachment B

RELEVANT TOPICS FOR EDUCATIONAL MATERIAL ON SPECIFIC REQUIREMENTS FOR MITC-GENERATING CHEMICALS SOURCES OF INFORMATION

The registrant Fact Sheets need to cover the following topics as a minimum. Additional information may be included. Flexibility in formats and length is acceptable. The information should be stated in plain, clear and understandable language. It should assist users to handle the chemicals correctly and safely and to understand the rationale for safe handling procedures. It should assist equipment builders and sellers to understand the equipment features required to minimise exposure.

Information should be aided where necessary with diagrams or photographs.

Further sources of information for registrants include the TGA reports (1995, 1996), Industry reports and product literature and the published literature, including studies cited in the OHS report.

Health effects

- Describe the health effects of metham, dazomet and MITC, including the following information. MITC is extremely irritating to the skin and mucous membranes and can also cause asthma-like lung allergy and skin allergy. MITC is capable of inducing symptoms at concentrations below the odour threshold. It can also be absorbed through the skin. Following a large environmental metham spill, the local population reported health effects including non-specific neurologic complaints (headache and dizziness) and irritation (eye, respiratory tract and skin); some affected persons progressed to persistent irritant-induced asthma.

- At present, the minimum and maximum MITC exposures that humans can tolerate have not been defined, nor have methods for biological monitoring.

- Workers previously adversely affected from contact with metham, dazomet and MITC residues should not work with MITC-generating chemicals.

- Anyone experiencing skin reddening, rashes, blisters or other symptoms should seek medical treatment. Symptoms from exposure can take some days to develop.

Personal protective equipment (PPE)

- PPE requirements exist for workers applying, sealing, re-handling treated soil and re-entering treated areas. The importance of preventing metham or dazomet from contaminating skin needs to be emphasised. Users should be aware that MITC permeates rubber, so specific glove materials are provided on the labels. Leather boots and gloves should not be used. Given the corrosive nature of MITC, careful maintenance of PPE is essential for adequate protection. Describe the equipment maintenance and cleaning required. For example, gloves, apron, footwear and respirator should be cleaned after each working day and checked for leaks and corrosion. Respirator filters should be well maintained and changed as required. Applicators should prevent granules and liquid drips from running into boots. Granules must not be dispensed by an ungloved hand. Any metham spills on skin or clothing should be dealt with immediately by washing skin or changing into clean clothing.

Work practices

- Workers should only handle freshly prepared solutions of metham because MITC fumes are produced on standing. Unused diluted solution should be discarded at the end of the day or operation.

- Ventilation requirements for greenhouse use. When products are used in greenhouses, thorough ventilation is essential during and after application. The highest MITC levels occur shortly after application of metham or dazomet. There are re-entry conditions for areas treated with metham and dazomet; these are specified on the label.

- MITC residues will be lower in well ventilated areas. Users should store, mix and apply metham and dazomet in well ventilated areas. This applies to greenhouses in particular, especially during the application and re-entry periods.

Application conditions

- Use of metham and dazomet under optimal environmental conditions and by targeted applications is of direct and indirect benefit to occupational health and safety. Unnecessary use, overuse, ineffective sealing or use under adverse environmental conditions would be minimised, as would unnecessary worker exposure to both the products and MITC residues.

- Describe the environmental conditions such as soil temperature and moisture necessary for efficacious use of metham and dazomet, and plant back instructions.

- Emphasise the mode of action of metham/dazomet, the conversion to poisonous MITC fumes and the influence of soil and environmental conditions on MITC production and subsequent degradation. Ineffective or delayed sealing of metham and dazomet can result in MITC fumes extending from the treatment area to neighbouring properties.

Application equipment

- Discuss the preferred equipment for field, greenhouse and other applications, namely an enclosed design that minimises worker exposure to the product or MITC residues. The end use scenarios would need to be considered. For instance, direct soil injection techniques rather than above ground applications with secondary soil incorporation, are preferable. Only certain use patterns are now permitted. For instance controlled irrigation application via low volume trickle systems under plastic is permitted but not high volume uncontrolled flood and overhead sprinkler systems with high potential for vaporising and drift. Enclosed metham potting mix treatments in well-ventilated areas are permitted but not open spraying. State and territory regulations regarding off-site effects should be included.

- Describe additional design features on equipment and hoses that can reduce metham leaks and exposure. These include anti drip devices, blowthrough equipment on injectors and improved systems for filling injectors.

- Automatic dispensing equipment particularly for large metham containers would be preferred. The options for this would need to be discussed.

- Workers should be more protected from MITC when using closed tractor cabs with airconditioning and chemical filters. However, the effectiveness of exposure control is highly dependent on the adoption of good occupational hygiene within the cabin. Some studies have shown that contamination of enclosed cabins can result in higher MITC than found in outside air. Training needs to emphasise that cabins and equipment should be kept clean, contaminated protective clothing, including gloves is not taken inside the cab, the door and windows are to be kept closed, including when temporarily when outside the cab during applications, and the filters well maintained. Breakthrough of fumes will alert users to ineffective control measures, however, it should be emphasised that indications are that MITC can cause health effects before odours or fumes are noticed.

- Procedures for dealing with equipment malfunctions. For example, leaks should be attended to without delay, while wearing the specified PPE.

- Plastic sheeting varies in permeability to MITC. Only a type and thickness impermeable to MITC should be used. Low density polyethylene has been shown to be ineffective in retaining MITC. This technical information should be available from registrants. Plastic sheeting should be in good repair and weighted down over treated soil.

OH&S Assesssment Report of Metham-Sodium (Root Inhibitor Use)

1. INTRODUCTION

This report (Part 2) considers the metham-sodium (referred to in this report as metham) product currently registered in Australia as a root inhibitor in sewer lines. It assesses the end use situation and makes recommendations on its future use.

Methylisothiocyanate (MITC) is also considered, being the active component of metham.

Information was obtained from the registrant of the product (ICI Australia Operations Pty Ltd (ICI) information received October 1995) and the Therapeutic Goods Administration (TGA) Toxicology Reports (TGA, 1995, 1996). The original submission for registration was not available from the National Registration Authority for Agricultural and Veterinary Chemicals (NRA).

This report should be read in conjunction with Part 1.

1.1 Overseas regulatory status

United States

As of March 1996, the US EPA classified all metham sewer products as restricted use pesticides, due to "the elaborate and complicated methods of applying this chemical and the potential for harmful human exposure". The agency considers it a difficult product to use that requires special training (Pesticide and Toxic Chemical News, 1994 and The Bureau of National Affairs Inc., 1994). In the US, these products can only be used by or under the direct supervision of certified applicators.

2. TOXICITY

Refer to Part 1 for details.

3. OCCUPATIONAL EXPOSURE

3.1 Registered product

Sanafoam Vaporooter (referred to in this report as Vaporooter) is the only metham product currently registered in Australia for use in sewers. The product is a suspension concentrate containing 228 g/L metham as the sodium salt, 26% of a foaming agent and 62% water. It is packed in 1 L high density polyethylene containers and 20 L closed head tin plate drums.

3.2 Estimated number of end users

The Vaporooter label indicates that the product is to be sold and used only by plumbers, drainers and sanitary engineers and other operators trained in the use of the product. All personnel involved in its application are trained by ICI, and hold a current certificate as a trained applicator of the product. This training includes standard and emergency procedures. The registrant indicates that four contract companies use the Vaporooter throughout Australia.

3.3 Use pattern

The information in this section derives from the Vaporooter label. Vaporooter is mixed with Nufarm Rootfoam S Herbicide (850 g/kg dichlobenil, wettable powder) and water, in a 5% solution (1.14% metham, 0.11% dichlobenil) and applied as a foam (0.057% metham v/v, 0.0056% dichlobenil w/v).

The quantity of foam required to treat the affected length of sewer line (including relevant household connections) is calculated by multiplying the pipe length by the quantity of foam required per metre. It is applied using dedicated equipment. ICI indicate that applicators in Australia use Airrigation Engineering Co., Inc. equipment (brochures provided in Appendix 6 of the ICI submission) or approved alternatives. The ICI submission (Appendix 5) includes copies of the Airrigation Engineering Co., Inc. Users Manual and Applicator's Training Manual, for the USA product.

Nufarm Rootfoam S Herbicide is added at 530 g per 20 L drum of Vaporooter. The herbicide is added directly to the drum containing the Vaporooter. The drum is re-capped and agitated by rolling. The required quantity is measured and mixed with sufficient water to make a 5% solution and loaded onto the foaming machine.

The first section to be treated is plugged at the manhole at the upstream end. The plug used should be adapted to receive the hose connection from the foam generator and pass the foam through the plug. The plug should also resist the back pressure of the foam (usually no more than 200 kPa). The foam is forced down the line until it appears at the other end of the line being treated. The procedure can be repeated in sections that have root growth downline.

The product can be used either downflow or upflow, on normal or hillside grades. Until root infested collection lines have all been cleared, it is recommended that treatment is carried out down stream.

3.4 Worker exposure studies

ICI submitted two reports on trials using Vaporooter in response to the data call-in by the NRA.

Study 1

Sheers R (1994) Melbourne Water - Sanafoam Vaporooter Trial, 7 November 1994.

The main objectives of the trial were:

- to understand the risks to deep sewer workers, particularly from exposure to MITC; and

- to be able to recommend suitable administrative controls for the safe use of this product in sewers.

The trial was conducted over several locations. The temperature was about 12°C with windy conditions. The Vaporooter was applied in one or two stages at each site.

The trial subjects were all trained and certified users of the product. They wore overalls (description not available) and nitrile gloves under thick lined rubber gloves. They used dedicated equipment mounted on a truck. The truck was positioned over the manhole and the product applied by jetting a hose in the sewer to the upstream manhole. The hose was slowly retrieved while pumping a trail of foam that completely filled the pipe. The raw material was stored on the back of the truck as concentrates and mixed with water just prior to application.

Personal monitoring was conducted at all sites while static sampling was carried out only at one site. Samples were obtained from the breathing zone of the applicator, at the point of application, a point two manholes (approximately 300 metres) down stream and a re-test at the point of application 24 hours later. Static sampling was carried out using a portable gas chromatograph and charcoal tubes. A field blank was used to detect contamination. Results are presented in Table 1.

After treatment, the operator used his gloved hand to clean the last few meters of hose (contaminated with foam) as it left the manhole and before it reached the hose reel.

In the absence of a NOHSC and ACGIH exposure standard for MITC, the study author used a Russian occupational exposure standard of 0.1 mg/m^3 (STEL) with a skin notation. The author assumed this to be a 15 minute TWA and concluded that this value incorporated a sufficient safety factor over the NOEL established in animal studies. The validity of this exposure standard or assumption cannot be assessed.

Table 1: Results of personal and static monitoring for airborne MITC

Sample	MITC concentration (mg/m^3)	MITC (mg/kg bw (a)
Study 1		
Operator breathing zone exposure (c)	0.8 (d)	0.133
At point of application	65.3 (d)	10.883
Two manholes downstream (approx. 300 m)	0.05	0.008
At point of application - 24 hours post-application	0.07	0.011
Study 2		
Operator breathing zone exposure	<0.05	<0.008
Operator breathing zone exposure	<0.08	<0.013
Operator breathing zone exposure	0.17	0.028
At point of application - 30 mins post application (e)	7.7 (d)	1.283
At point of application - 90 mins post application (e)	3.9 (d)	0.650
At point of application - 180 mins post application (f)	20.2 (d)	3.366
At point of application - 270 mins post application (f)	13.2 (d)	2.200
At point of application - 360 mins post application (f)	2.6 (d)	0.433
At point of application - 24 hours post-application (f)	<0.03	0.005

Source: Sheers R (1994) Melbourne Water - Sanafoam Vaporooter Trial, 7 November 1994 and Sheers R (1995) Melbou February 1995, ICI Australia Operations Pty Ltd.

(a) Assumes a breathing rate of 10 m^3 per working day; average body weight of 60 kg
(b) MOE based on the human dose (3.56 mg/kg bw/day) equivalent to the NOEL derived from a three month rat inhalatio worker
(c) Sampling time 65 minutes, corresponding to the time the Vaporooter was being pumped
(d) Values exceed the eye irritation threshold in cats of 0.2 mg/m^3
(e) Manhole cover left completely open
(f) Manhole cover open approximately 2 cm

Results

The concentration of MITC was above the exposure limit at the point of application. However, the MITC was confined to the application area because the concentration of MITC was below the exposure standard two manholes away. In addition, the level of MITC fell below this exposure standard at the application site within 24 hours. The field blank did not show any contamination.

The study suggested that the high level of MITC at the time of application could have occurred during the time the hose was retrieved from the manhole and from minor leaks in pressurised lines in the back of the truck. The next study tests this theory.

The study also concluded that an exclusion period of at least 24 hours is appropriate to enable MITC levels to fall below acceptable levels as defined by the Russian exposure standard.

Improved work practices and maintenance of equipment were recommended.

Study 2

Sheers R (1995) Melbourne Water - Sanafoam Vaporooter Trial, 13-14 February 1995, ICI Australia Operations Pty Ltd.

The main objectives of the trial, relevant to this assessment, were as follows:

- to establish the rate at which the concentration of MITC in the sewer reduces with time, to a level below the recommended hygiene limit; and

- To conduct personal monitoring of the applicator to establish the effectiveness of controls, introduced since the last trial, to reduce exposure.

The details of operator and truck were identical with Trial 1. The temperature on both days was approximately 30°C with fairly still conditions. The product was applied in three stages. Personal monitoring (breathing zone) was conducted during the three applications. The sewer samples were taken during the first application only, about 1 metre above the foam in the manhole. MITC levels were measured in the sewer at 1-2 hour intervals after application. Results are provided in Table 1.

Improved work practices were adopted following Study 1 and the contaminated application hose was cleaned using a stream of water rather than the operator’s gloved hand.

The exposure standard described in Study 1 was utilised.

Results

Results of personal monitoring indicated that the controls introduced since Trial 1, ie. use of water to wash the contaminated hose instead of the worker's gloved hand, reduced applicator exposure by inhalation to MITC by approximately 10 fold.

The concentration of MITC in the sewers declined rapidly within 24 hours. MITC declined sharply from 0 - 6 hours. However, insufficient data was collected to refine the re-entry period less than 24 hours.

The study concluded that an exclusion period of at least 24 hours was still appropriate for the treated pipe. If entry is required within this time it recommended an organic vapour respirator with a full face mask for entry between 6-24 hours and an air supplied mask for entry within 6 hours of treatment.

4. RISK ASSESSMENT

The risk assessment considers metham and MITC exposure for workers involved in mixing/loading and applying the product, cleaning up spills and equipment and re-entering treated sewers.

4.1 Dermal absorption

In the absence of dermal absorption data for metham and MITC, the occupational health and safety (OHS) report uses a default value of 10% (refer to Part 1 for details).

4.2 Acute toxic potential

The main acute hazards of metham are moderate dermal toxicity, corrosion of skin, severe eye irritation and strong skin sensitisation. The main hazards of MITC are moderate dermal and inhalation toxicity, severe skin irritation, corrosion to eyes, respiratory irritation and moderate skin sensitisation.

The acute dermal LD_{50} for metham sodium is 650 mg/kg. For a 60 kg worker, this corresponds to a dermal exposure of 171 mL of undiluted Vaporooter, 3.4 L of the working strength solution and 68 L foam. This calculation does not consider exposure to MITC and does not include a safety factor.

Vaporooter is mixed with dichlobenil prior to use. Dichlobenil is of low acute oral toxicity (oral LD_{50}: 3160 mg/kg, rat) and moderate acute dermal toxicity (dermal LD_{50}: 1350 mg/kg, rabbit). Its acute inhalation toxicity is unknown (Hayes and Laws, Ed., 1991). It is non-irritant to eyes and skin and non-sensitising to skin (ICI Material Safety Data Sheet (MSDS) for dichlobenil). The final concentration of dichlobenil in the foam is 0.0056% (w/v), so it is not expected to affect the overall acute toxicity of the mixture.

The acute dermal and inhalation toxicity plus the irritant effects of metham and MITC, indicate that skin and respiratory protection is necessary for workers handling the concentrate, working strength solution and foam. This protection is appropriate to minimise skin contamination with dichlobenil.

4.3 Repeat dose toxic potential

It is anticipated that workers trained in the use of this product would treat sewers on a regular basis, under ongoing sewer maintenance programs.

Exposure to metham

The only available NOEL for metham is 10 mg/kg/d established in developmental studies using rat (for maternotoxicity and foetotoxicity) and rabbit (for embryotoxicity). For a 60 kg worker, assuming 10% dermal penetration for metham, a daily dermal exposure of more than 6000 mg metham, 26.3 mL of undiluted Vaporooter, 526 mL of the working strength solution or 10.5 L foam, is needed to exceed the NOEL. This calculation does not include a safety factor.

Contamination with undiluted Vaporooter is not likely to be tolerated due to the corrosion of the product, hence workers are expected to wash off spills quickly.

Exposure to MITC

It is possible that workers repeatedly handling the product may be exposed to MITC as a conversion product, in metham solutions, from metham breakdown on contaminated skin, or through environmental (airborne) exposure at application.

The inhalation NOEL for MITC from a 3 month rat study is 30.7 mg/m^3 based on clinical signs. This is equivalent to 3.56 mg/kg (assuming a minute volume of 29 L/min, 4 hour exposure per day) for a 60 kg worker. The quantity of MITC generated from metham will vary depending on environmental and other factors. Hence, it is not possible to provide an equivalent theoretical dose of metham.

Exposure to dichlobenil

Available data indicates that dichlobenil is of low repeat dose toxicity. A 21 day dermal study in rabbits indicated a no-effect-level of 100 mg/kg/d. There is some evidence to suggest that dichlobenil may cause dermatitis following occupational exposure (Hayes and Laws, Ed., 1991). Dichlobenil is present at one tenth the concentration of metham. Comparing NOELs and the dermal protection factor for metham, the risk from repeat dose exposure is lower than that of metham. Therefore, the presence of dichlobenil is not expected to significantly alter the toxicity of the mixture.

4.4 Assessment of end use exposure studies

Margins of exposure (MOE) were generated from the airborne MITC residues measured in the two worker studies. They are related to an 8 hour exposure (10 m^3/day) and the MITC inhalation NOEL, converted to mg/kg bw/d. They are included as an indicator of the risk associated with systemic toxicity.

During the application, airborne MITC by personal air sampling was above the selected exposure limit in the one instance tested in Trial 1 (MOE= 27). When measures were introduced to eliminate the need for workers to manually clean metham foam from the hose (Trial 2), airborne MITC by personal air sampling was below the exposure limit in two of the three cases and MOE = >445, >274 and 127.

The MITC residues in the operator's breathing zone were compared with the most sensitive sign of MITC exposure, 0.2 mg/m^3, ocular mucosal irritation in the cat (Nesterova, 1969, cited in Alexeeff et al., 1994). The operator in Study 1 exceeds this value and one operator in Study 2 approximates it at 0.17 mg/m^3. These two workers also exceed the Alexeeff et al. (1994) Reference Exposure Level to prevent disability of 0.13 mg/m^3 over a one hour exposure.

The extent to which the change in procedures was responsible for the reduced airborne residues cannot be determined. Only one worker was monitored in Trial 1 and only three in Trial 2. Both trials were conducted in different weather conditions; this may also have influenced airborne MITC. It is not clear if the operator monitoring included the mixing process, an activity for which the label states the operator should wear a respirator and goggles. No comments are made whether or not the operators experienced odours or fumes.

Only airborne concentrations of MITC were measured in both trials. Hence, no conclusions could be drawn regarding the adequacy of skin protection worn by applicators.

The limited number of operators monitored does not provide sufficient information to conclude that respiratory protection is not required when applying the foam, particularly as there is no approved Australian exposure standard. In fact, comparison with irritation thresholds indicates that eye and respiratory protection should be provided.

4.5 Assessment using exposure calculation models

Worksafe Australia did not use the exposure calculation model Predictive Operator Exposure Model (POEM) to extrapolate end user exposure because the model does not simulate the application method for Vaporooter.

4.6 Conclusions on worker exposure to Vaporooter

No information is available to assess worker dermal contamination with metham and/or MITC when using Vaporooter. Extensive personal protective equipment is needed to protect workers against the topical effects of metham/MITC.

Information to assess the risk of metham/MITC odours and fumes and systemic inhalation exposure is limited. Available data does not comment on the existence of odours or fumes in normal circumstances. ICI worker studies suggest that a reduction in manual handling of

equipment contaminated with metham foam may reduce exposure to airborne MITC. ICI should continue improvement of engineering controls to reduce the reliance on extensive personal protective equipment (PPE). The studies do not mention if the mixing/loading stage is included in the monitoring period. In the absence of information, workers handling Vaporooter should adopt respiratory and eye protection for the entire mixing/loading/application/clean-up process.

4.7 Personal protective equipment indicated by the risk assessment

The personal protective equipment required to protect end users against health effects following acute and repeated exposure is given in Table 2.

Table 2: Personal protective equipment required in Safety Directions resulting from acute and repeat dose risk assessment

Risk assessment	Personal protective equipment (tasks)
Acute risk Section 4.2	
• acute lethal dermal toxicity (metham and MITC)	elbow-length (nitrile, neoprene) gloves, cotton overalls buttoned to the neck and wrist, a washable hat (when opening containers, preparing and applying foam). In addition, chemical resistant apron (when opening containers and preparing foam)
• acute lethal inhalation toxicity (metham and MITC)	full facepiece respirator with organic vapour/gas cartridge or canister [or goggles and half facepiece respirator with organic vapour/gas cartridge or canister] (when opening containers, preparing and applying foam)
• eye irritation (metham and MITC)	full facepiece respirator or goggles (when opening containers, preparing and applying foam)
• skin irritation (metham and MITC)	elbow-length (nitrile, neoprene) gloves, cotton overalls buttoned to the neck and wrist, a washable hat, chemical resistant footwear (when opening containers, preparing and applying foam). In addition, chemical resistant apron (when opening containers and preparing foam)
• skin sensitisation (metham and MITC)	as above
Repeat dose risk	
• worker study Section 4.6 (systemic toxicity)	full facepiece respirator with organic vapour/gas cartridge or canister [or goggles and half facepiece respirator with organic vapour/gas cartridge or canister] (when opening containers, preparing and applying foam)

4.8 Re-entry assessment

The product label does not include a re-entry restriction.

Monitoring of airborne MITC during the 24 hours after treatment in Trial 2, shows that MITC levels peak at 3 - 4.5 hours, then decline sharply. Corresponding MOE are very low (1-8) over the period 30 min - 6 hours after treatment. The fate of MITC residues between 6 - 24 hours was not followed.

In the two trials, airborne MITC was higher than the most sensitive irritant threshold (0.2 mg/m^3, cats) within the treated manhole for at least 6 hours and for some time between 6 - 24 hours after application.

Both ICI Trials indicate that a re-entry period of 24 hours may be adequate when airborne MITC is compared with the irritant threshold. Furthermore, MOE based on the three month inhalation study in rats, converted to mg/kg bw/d, are high at this time in the treated manhole (324 and 712 for Trial 1 and 2 respectively). It is noted that, in Trial 2, samples were collected after the manhole cover was left open for 90 minutes, then partly open up to 24 hours. This may have influenced dissipation of MITC and it is unknown if this is standard practice. There was no information provided by ICI on the extent to which workers experience odours or fumes if they enter treated sewers at 24 hours.

Trial 2 suggests that re-entry at times 0 - 6 hours would require an air supplied respirator, 6 - 24 hours would require a full face respirator with organic vapour cartridge and >24 hours would not require respiratory protection unless it were otherwise indicated.

Trial 1 showed low airborne MITC at a point 300 meters distant from the point of application. The time relative to application is not given and the possibility that MITC may infiltrate over time is not investigated. From this data it is not possible to specify a safe working distance for other workers.

4.9 Tank mixing

The presence of dichlobenil in the working solution and foam does not influence the protective clothing requirements or re-entry requirements.

5. REGULATORY CONTROLS

5.1 Statement of Hazardous Nature

The Statement of Hazardous Nature for metham specified in Part 1 applies to Vaporooter.

5.2 Exposure standards

The Exposure Standards section in Part 1 for metham applies to Vaporooter. In addition, in considering whether to establish an Exposure Standard for MITC, the NOHSC Exposure Standards Expert Working Group should take into account the use of Vaporooter in confined spaces.

Sodium hydroxide, an ingredient in Vaporooter, has a NOHSC exposure standard of 2 mg/m^3 time weighted average (NOHSC 1995).

6. WORKSAFE AUSTRALIA RECOMMENDATIONS TO THE NRA

6.1 Exposure standards

Rec (1) The recommendation in Part 1 of this report is relevant for Sanafoam Vaporooter.

6.2 Use

The existing use of Sanafoam Vaporooter is supported.

6.3 Training and information provision; restriction on availability and registration conditions

The Sanafoam Vaporooter label states that the product is "to be sold and used only by plumbers, drainers and sanitary engineers and operators trained in the use of this product". ICI Australia Operations Pty Ltd provides the formal training to the four contract companies using the product in Australia.

The assessment supports the need for special training in the use of Sanafoam Vaporooter, because of the hazards for applicators and re-entry workers and as special equipment and work practices are necessary for safe use. In particular, training needs to be kept up-to-date so that users are informed of recommended modifications to work practices or equipment.

The Sanafoam Vaporooter material safety data sheet submitted for review needs upgrading to meet NOHSC requirements.

Rec (2) Sanafoam Vaporooter should only be used by persons with adequate training. The present ICI Australia Operations Pty Ltd training arrangements may be adequate for the current registered product, subject to Rec 3. The NRA needs to ensure a mechanism exists for this training requirement, if necessary by scheduling Sanafoam Vaporooter as a restricted chemical product by regulation, consistent with Part 1 - Rec 6.

Rec (3) The NRA to determine whether company training is an appropriate and feasible basis for restricting access to the product and require a mechanism for ensuring an adequate training program, including upgrades. For example, companies could be required to lodge training programs with the NRA as a condition of registration. Such programs must include the mechanism for ensuring improved work practices, for example, those concerned with occupational hygiene, are incorporated in training programs and also passed on to contractors.

Rec (4) The NRA advise the registrant that the Sanafoam Vaporooter MSDS is to be amended to meet NOHSC requirements and submitted to Worksafe Australia for assessment.

6.4 Safety directions

Rec (5) The safety directions for metham-sodium SC 510 g/L or less are appropriate for this product. Refer to Part 1 for details.

6.5 Product Label

Rec (6) Sanafoam Vaporooter is a hazardous substance and requires a reference to the MSDS on the label.

Rec (7) The following label precaution statements are required. They should be located directly under the safety directions.

> Workers previously experiencing skin or respiratory tract irritation from metham-sodium exposure should not work with metham-sodium products.
>
> After mixing with water do not allow mixture to stand as poisonous fumes are released on standing.

Rec (8) The following label re-entry statement is required on the product label. It should be located directly under the safety directions.

> **Re-entry period**
> Do not allow entry into treated areas for 24 hours after treatment. When prior entry is necessary, wear protective equipment specified in the safety directions for applicators, except for entry within 6 hours when an air supplied respirator is required. Clothing must be laundered after each day's use.

6.6 Exposure to other workers

Limited information was provided by ICI Australia Operations Pty Ltd on the distribution of MITC residues from the point of application on the surface or within the sewer system. This has implications for the safety of other workers nearby.

Rec (9) The NRA seek further advice or data from ICI Australia Operations Pty Ltd on the nomination of safe working distances from the point of application to other sewers located nearby and a buffer area around the application site.

Rec (10) The NRA clarify with ICI Australia Operations Pty Ltd the mechanism for restricting access by other workers to treated areas, adjacent sewers and the application site.

7. REFERENCES

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WORKSAFE AUSTRALIA RECOMMENDATIONS TO THE NRA -

PART 2

Metham sodium sewer use

Exposure standards

Rec (1) The recommendation in Part 1 (refer above) is relevant for Sanafoam Vaporooter.

Use

The existing use of Sanafoam Vaporooter is supported.

Training and information provision; restriction on availability and registration conditions

The Sanafoam Vaporooter label states that the product is "to be sold and used only by plumbers, drainers and sanitary engineers and operators trained in the use of this product". ICI Australia Operations Pty Ltd provides the formal training to the four contract companies using the product in Australia.

The assessment supports the need for special training in the use of Sanafoam Vaporooter, because of the hazards for applicators and re-entry workers and as special equipment and work practices are necessary for safe use. In particular, training needs to be kept up-to-date so that users are informed of recommended modifications to work practices or equipment.

The Sanafoam Vaporooter material safety data sheet submitted for review needs upgrading to meet NOHSC requirements.

Rec (2) Sanafoam Vaporooter should only be used by persons with adequate training. The present ICI Australia Operations Pty Ltd training arrangements may be adequate for the current registered product, subject to Rec 3. The NRA needs to ensure a mechanism exists for this training requirement, if necessary by scheduling Sanafoam

Vaporooter as a restricted chemical product by regulation, consistent with Part 1 - Rec 6.

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Exposure to other workers

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Rec (10) The NRA clarify with ICI Australia Operations Pty Ltd the mechanism for restricting access by other workers to treated areas, adjacent sewers and the application site.